Variation in Conditions and Global Practice Patterns in Patients Initiating Dialysis

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KDIGO Controversies Conference on Advanced CKD
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DOPPS Program Area

Three Major Projects, One Common Goal

- CKDopps (advanced CKD)
  - Brazil
  - France
  - Germany
  - USA
  - Japan

- DOPPS (hemodialysis, since 1996)
  - Canada
  - Belgium
  - France
  - Germany
  - Italy
  - China
  - Japan
  - Spain
  - Sweden
  - UK
  - USA
  - GCC-6
  - Turkey
  - Russia

- PDOPPS (peritoneal dialysis)
  - Australia
  - Canada
  - Japan
  - Thailand
  - New Zealand

Arbor Research Collaborative for Health
Global Practice Patterns at Dialysis Start

Outline

• Framing data:
  – Age, mortality, practice variation

• Need to improve practices:
  – Vascular access

• Need to prioritize patient choice:
  – Modality selection & withdrawal

• Preliminary CKDopps data:
  – Poor performance against KDIGO
Framing Data

Age, mortality, practices at time of dialysis transition
Key Practice Changes & Impact

Burden of Dialysis (HD)

• Good news: Stable incidence rates, declining mortality on dialysis

• Realities: Rising incidence counts, prevalent counts, and age on dialysis = higher societal burden

• Access to modalities other than ICHD is too low, in US and elsewhere

Age Trends by Country
DOPPS 2-5 (2002-2013)

Mean age (years)

**Non-European Countries**

**European Countries**

Study Year

Mean age (years)
# Age Comparison: US to Japan

Table: Mean age among ESKD patients

<table>
<thead>
<tr>
<th></th>
<th>1996</th>
<th>2013</th>
<th>Change over time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>JSDT:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New patients</td>
<td>62</td>
<td>69</td>
<td>+7</td>
</tr>
<tr>
<td>All patients</td>
<td>59</td>
<td>67</td>
<td>+8</td>
</tr>
<tr>
<td><strong>USRDS:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New patients</td>
<td>60</td>
<td>62</td>
<td>+2</td>
</tr>
<tr>
<td>All patients</td>
<td>54</td>
<td>59</td>
<td>+5</td>
</tr>
</tbody>
</table>

In Japan
38% of new dialysis patients are age 75+
32% of all dialysis patients are age 75+

JSDT. Therapeutic Apheresis and Dialysis 2015;19:540-574
USRDS ADR reference tables, 2015

Mortality rate (deaths per 100 patient years)

- ≤120 days
- 121-365 days
- >365 days
Association of mortality with age and vintage

Hazard ratio†

| Ref. | 1.08 | 1.24 | 1.55 | 1.53 | 1.59 |

Mortality rate*

| ≤120 days | 6.0 | 11.4 | 17.4 | 28.2 | 45.6 |
| 121-365 days | 6.4 | 8.3 | 12.1 | 16.9 | 28.5 |
| >365 days | 4.8 | 7.2 | 10.1 | 15.5 | 25.7 |

† Models were adjusted for age, sex, race, and diabetes as cause of ESRD, stratified by countries and study phase, and accounted for facility clustering.

* Mortality rate: unadjusted number of deaths per 100 patient-years. Error bars correspond to 95% confidence intervals calculated using the Byer approximation.

Figure 6.2.a Adjusted all-cause mortality (deaths per 1,000 patient-years) by treatment modality, cohort (year of ESRD onset), and number of years after start of dialysis among incident hemodialysis patients, 1996, 2001, 2006, and 2011

Data Source: Special analyses, USRDS ESRD Database. Adjusted for age, sex, race, and primary diagnosis. Reference population: period prevalent ESRD patients, 2011. Abbreviation: ESRD, end-stage renal disease.
Vascular access use\textsuperscript{a} – incident patients

DOPPS 5 (2012-2014)

\textbf{% of Patients}

\begin{tabular}{c|c|c|c|c}
& Other & Catheter & AV-Graft & AV-Fistula \\
\hline
Jpn & 11 & 5 & 84 & 66 \\
Tur & 34 & 42 & 58 & 56 \\
Ita & 42 & 47 & 53 & 51 \\
Ger & 49 & 50 & 48 & 45 \\
UK & 50 & 42 & 55 & 50 \\
Spa & 50 & 10 & 7 & 5 \\
Rus & 50 & 42 & 67 & 68 \\
Swe & 50 & 45 & 71 & 71 \\
A/NZ & 50 & 44 & 67 & 68 \\
Chi & 28 & 28 & 23 & 19 \\
US & 50 & 42 & 67 & 68 \\
Can & 50 & 42 & 67 & 68 \\
Bel & 50 & 42 & 67 & 68 \\
GCC & 50 & 42 & 67 & 68 \\
\hline
\end{tabular}

N Patients: 149 13 59 120 40 123 36 81 11 50 334 68 53 73

\textsuperscript{a}At study entry for patients on dialysis ≤60 days at DOPPS enrollment

KDIGO 2012
Initiate dialysis for s/sx of uremia,
uncontrolled volume status, or
refractory nutritional decline; this
often occurs at eGFR 5-10 ml/min/m²

Adapted from Bieber et al. ASN abstract (2013)
eGFR at dialysis initiation
DOPPS 4.5 (2009-2015)

% of patients

<table>
<thead>
<tr>
<th>Region</th>
<th>&lt; 5.0 mL/min/1.73m^2</th>
<th>5.0-9.9 mL/min/1.73m^2</th>
<th>10+ mL/min/1.73m^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bel</td>
<td>59</td>
<td>55</td>
<td>50</td>
</tr>
<tr>
<td>Tur</td>
<td>58</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>Ger</td>
<td>55</td>
<td>47</td>
<td>33</td>
</tr>
<tr>
<td>US</td>
<td>50</td>
<td>40</td>
<td>33</td>
</tr>
<tr>
<td>Can</td>
<td>43</td>
<td>47</td>
<td>33</td>
</tr>
<tr>
<td>A/NZ</td>
<td>50</td>
<td>51</td>
<td>33</td>
</tr>
<tr>
<td>Spa</td>
<td>43</td>
<td>51</td>
<td>33</td>
</tr>
<tr>
<td>UK</td>
<td>33</td>
<td>62</td>
<td>28</td>
</tr>
<tr>
<td>Fra</td>
<td>28</td>
<td>27</td>
<td>24</td>
</tr>
<tr>
<td>Ita</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Swe</td>
<td>24</td>
<td>60</td>
<td>23</td>
</tr>
<tr>
<td>Jpn</td>
<td>24</td>
<td>61</td>
<td>23</td>
</tr>
<tr>
<td>Chi</td>
<td>24</td>
<td>60</td>
<td>23</td>
</tr>
<tr>
<td>Rus</td>
<td>18</td>
<td>58</td>
<td>20</td>
</tr>
<tr>
<td>GCC</td>
<td>18</td>
<td>51</td>
<td>20</td>
</tr>
</tbody>
</table>

N Pts:
Bel 308 Tur 562 Can 562 US 401 A/NZ 92 Fra 144 Swe 367 Jpn 527 Chi 136 Rus 213 GCC 213

Mean:
Bel 11.8 Tur 11.5 Can 9.8 A/NZ 9.1 US 10.9 UK 8.9 Fra 8.6 Swe 7.9 Jpn 7.5 Chi 7.2 Rus 6.8 GCC 6.3

Adapted from Bieber et al. ASN abstract (2013)
Figure 1.22  Trends in the distribution (%) of eGFR (ml/min/1.73 m2) among incident ESRD patients, 1996-2014

Data Source: Special analyses, USRDS ESRD Database. Population only includes incident cases with CMS form 2728. eGFR calculated using the CKD-EPI equation (CKD-EPI eGFR (ml/min/1.73 m2) for those aged ≥18 and the Schwartz equation for those aged <18. Abbreviations: CKD-EPI; chronic kidney disease epidemiology calculation; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease.
Need (Imperative!) to Improve Practices During the Dialysis Transition Period

Vascular Access
AVF maturation success*, by region

% of AVFs

N AVFs =

US | Europe/ANZ | Japan
---|------------|-------
1266 | 1022 | 472

*AVF maturation success was defined as use ≥ 30 days
Restricted to AVFs created in DOPPS 4 and 5 (2009-2015) in US, Europe, Australia and New Zealand, and Japan
Time to Primary Fistula Failure by Number Created by Surgeon During Training

![Graph showing the probability of first AVF failure over years since placement for different categories of AVF created during training. The graph includes a box with the statement: "Risk of failure 34% lower if created ≥ 25 (P=0.002)*."

* Adjusted for age, sex, race, vintage, 14 comorbidities, prior catheter use, country

Goodkin et al. AJKD 2010;56:1032

0-24 AVF
n=622

25-75 AVF
n=675

>75 AVF
n=660
Blood Flow Rate and Fistula Survival

HR of Final AVF Failure per 50 mL/min higher than the facility median BFR (95% CI)

Adjusted for age, sex, black race, BMI, vintage, cardiac disease, cerebrovascular disease, PAD, lung disease, cancer, psychiatric disease, and recurrent cellulitis, prior catheter use, and fistula location. DOPPS 2 and 3. n=2,132 fistulas. † Only 14 failure events in Japan.

AV Fistula location, by region and phase
DOPPS 1-5 (1996-2015)

% of AVFs

<table>
<thead>
<tr>
<th>Phase</th>
<th>Japan</th>
<th>Europe/ANZ</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>N AVFs:</td>
<td>2470 1885 1924 1834 2013</td>
<td>3162 4157 4161 4813 3321</td>
<td>2032 882 1096 4043 1617</td>
</tr>
<tr>
<td>N Fac:</td>
<td>65 59 62 58 58</td>
<td>100 162 152 154 145</td>
<td>142 80 63 138 72</td>
</tr>
</tbody>
</table>

Upper arm
Lower arm
Regional difference in **ESA dose** by vintage

Mean weekly ESA dose (units/week), among those treated with ESAs

DOPPS 5 (2012-2015); restricted cubic spline with 4 knots used to model vintage in each region

Karaboyas et al, ASN oral abstract (2016)
Need to Prioritize Patient Choice:
Modality Selection & Withdrawal
Renal replacement therapy modality use among prevalent ESKD patients, by country, in 2013

USRDS 2015 ADR, Vol. 2, Chapter 13 - International Comparisons
Education on treatment options for renal failure

US CKDopps (2015)

Which treatment would you choose if your kidneys failed completely in the next month?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Age &lt;70 (n=147)</th>
<th>Age ≥70 (n=195)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I don’t know</td>
<td>57%</td>
<td>61%</td>
</tr>
<tr>
<td>No treatment</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Kidney transplant</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>PD</td>
<td>22%</td>
<td>20%</td>
</tr>
<tr>
<td>Home HD</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>In-center HD</td>
<td>5%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Year 1 Patient Questionnaire data, among US patients with eGFR <30

CKDopps Patient Questionnaire; updated from Mariani et al (ASN 2015 abstract)
Proportion of Deaths due to Withdrawal from Dialysis by Dialysis Period and Country

% of death due to withdrawal

Countries were ordered by percent of deaths due to withdrawal from dialysis

CKDopps: Improving outcomes in advanced CKD and the transition to dialysis

Benedicte Stengel
on behalf of CKDopps and CKD-REIN Investigators

Inserm U1018, Univ Paris-Saclay
Centre for Research in Epidemiology and Population Health
Renal and Cardiovascular Epidemiology Team
Villejuif, France
The CKD Outcomes and Practice Patterns Study (CKDopps): Rationale and Methods

Laura Mariani, MD, MS, 1,2 Bénédicte Stengel, MD, PhD, 3
Christian Combe, MD, PhD, 4,5 Ziad A. Massy, MD, PhD, 3,6 Helmut Reichel, MD, 7
Danilo Fliser, MD, 8 Roberto Pecoits-Filho, MD, PhD, 9
Antonio A. Lopes, MD, MPH, PhD, 10 Kunihiro Yamagata, MD, PhD, 11
Takashi Wada, MD, PhD, 12 Michelle M.Y. Wong, MD, MSc, 1 Elodie Speyer, PhD, 1
Friedrich K. Port, MD, MS, 1,2 Ronald L. Pisoni, PhD, MS, 1 and
Bruce M. Robinson, MD, MS 1,2

Background: Minimizing clinical complications in patients with advanced chronic kidney disease (CKD) and improving the transition to dialysis therapy and transplantation represents a challenge, requiring reliable evidence regarding the effects of CKD care on outcomes.

Study Design: The CKD Outcomes and Practice Patterns Study (CKDopps) is a new international prospective cohort study designed to describe and evaluate variation in nephrologist-led CKD practices.
<table>
<thead>
<tr>
<th>Country</th>
<th>Sites Recruited Target</th>
<th>Sites Recruited</th>
<th>Patient Enrollment Target</th>
<th>Patients Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>20</td>
<td>20</td>
<td>1,600</td>
<td>946</td>
</tr>
<tr>
<td>France (CKD-Rein)</td>
<td>40</td>
<td>40</td>
<td>3,200</td>
<td>3,034</td>
</tr>
<tr>
<td>Germany</td>
<td>30</td>
<td>32</td>
<td>1,800</td>
<td>1,810</td>
</tr>
<tr>
<td>Japan</td>
<td>30</td>
<td>30</td>
<td>2,400</td>
<td>1,043</td>
</tr>
<tr>
<td>United States</td>
<td>40</td>
<td>30</td>
<td>3,200</td>
<td>1,380</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>160</strong></td>
<td><strong>152</strong></td>
<td><strong>12,200</strong></td>
<td><strong>8,213</strong></td>
</tr>
</tbody>
</table>

*derived from electronically transferred datasets

As of 11/1/2016
## Baseline patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Brazil</th>
<th>France</th>
<th>Germany</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, N</td>
<td>774</td>
<td>3034</td>
<td>1810</td>
<td>1057</td>
</tr>
<tr>
<td>Median age, year</td>
<td>67</td>
<td>69</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Women</td>
<td>48%</td>
<td>35%</td>
<td>43%</td>
<td>48%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>47%</td>
<td>40%</td>
<td>42%</td>
<td>59%</td>
</tr>
<tr>
<td>Median years of diagnosed CKD</td>
<td>2.2</td>
<td>5.0</td>
<td>-</td>
<td>3.2</td>
</tr>
<tr>
<td>Mean eGFR, mL/min/1.73 m²</td>
<td>25.7</td>
<td>33.8</td>
<td>27.6</td>
<td>26.7</td>
</tr>
</tbody>
</table>
Albuminuria or proteinuria monitoring by diabetes status

KDIGO 2.1.1 Assess albuminuria annually (Not Graded)

* requested lab per study protocol in France vs routine lab in other countries
RASi use, by CKD stage

% of patients

<table>
<thead>
<tr>
<th>Country</th>
<th>Stage 3a</th>
<th>Stage 3b</th>
<th>Stage 4-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>86</td>
<td>70</td>
<td>58</td>
</tr>
<tr>
<td>France</td>
<td>77</td>
<td>78</td>
<td>74</td>
</tr>
<tr>
<td>Germany</td>
<td>87</td>
<td>79</td>
<td>80</td>
</tr>
<tr>
<td>US</td>
<td>68</td>
<td>66</td>
<td>47</td>
</tr>
</tbody>
</table>

RASi: renin angiotensin system inhibitors, including ACEi, ARB and renin inhibitors
Patients reporting to have received advice to reduce protein intake

% of patients

<table>
<thead>
<tr>
<th>CKD stage</th>
<th>Brazil</th>
<th>France</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>44</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>3b</td>
<td>39</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>39</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>47</td>
<td>22</td>
</tr>
</tbody>
</table>

KDIGO 2012
Lowering protein intake to 0.8 g/kg/d with appropriate education (2B or 2C)
Global Practice Patterns at Dialysis Start

Outline

• Framing data:
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Thank you