Palliative Care in Chronic Kidney Disease: Past Successes, Remaining Challenges

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BC Nephrology Days, Vancouver, BC
Nov 6, 2009
Objectives

- Highlight the relevance of palliative/supportive care to ESRD.

- Describe successes in renal palliative care
  - Identification of the problem
  - Ethical guideline development
  - Framework to integrate renal palliative care
  - Advances in prognosis estimation and advance care planning
  - Pain and symptom assessment and management

- Present remaining challenges
  - Systematic integration of ACP
  - Symptom management (non-pain, spirituality)
  - Palliative care education for renal staff
  - Understanding of barriers to hospice for dialysis patients
  - Determining who will benefit from conservative management
Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

World Health Organization
Relationship between Palliative Care and End-of-Life Care
The ESRD Population

- Significant co-morbidity
- 50% patients starting dialysis > 65 yrs
- Patients ≥ 75 yrs: fastest-growing group of dialysis patients.
## Unadjusted Survival Probabilities (%) for Incident ESRD Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>5 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 - 49</td>
<td>89.6</td>
<td>81.6</td>
<td>73.5</td>
<td>61.9</td>
<td>37.7</td>
</tr>
<tr>
<td>50 - 59</td>
<td>86.2</td>
<td>75.9</td>
<td>65.4</td>
<td>49.5</td>
<td>21.8</td>
</tr>
<tr>
<td>60 - 64</td>
<td>83.0</td>
<td>69.6</td>
<td>58.3</td>
<td>38.1</td>
<td>12.3</td>
</tr>
<tr>
<td>65 - 69</td>
<td>79.1</td>
<td>63.1</td>
<td>50.8</td>
<td>30.7</td>
<td>6.4</td>
</tr>
<tr>
<td>70 - 79</td>
<td>71.2</td>
<td>53.5</td>
<td>39.0</td>
<td>20.2</td>
<td>2.7</td>
</tr>
<tr>
<td>80+</td>
<td>60.5</td>
<td>40.8</td>
<td>25.7</td>
<td>9.6</td>
<td>0.9</td>
</tr>
</tbody>
</table>

USRDS, 2008
Survival Rates for Cancer and ESRD Patients

Data from USRDS and NCI
Annual unadjusted mortality rate ~22%

Withdrawal from dialysis ~ 20-25% of deaths

The majority lack capacity at the time the decision to withdraw dialysis is made.

Only 6-51% of HD patients have advance directives
• Address only limited treatment options
• Typically do not address withdrawal of dialysis
• Most do not choose DNR

Dialysis patients typically do not view themselves as terminally ill
How EOL Decisions Are Being Made

- By family and health care providers
- Surrogates lack the knowledge of patients’ preferences
  - Includes wishes for ongoing dialysis
  - Family consistently overestimates patients’ desires to continue dialysis across hypothetical health conditions

<table>
<thead>
<tr>
<th></th>
<th>Current preferences for CPR</th>
<th>Wish for dialysis in a severely demented state</th>
<th>Wish for dialysis if they had terminal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family</td>
<td>50%</td>
<td>44%</td>
<td>47%</td>
</tr>
<tr>
<td>Physician</td>
<td>44%</td>
<td>47%</td>
<td>43%</td>
</tr>
</tbody>
</table>

Miura y et al. AJKD 2006
CPR Outcomes

- Moss 1992: 74 patients had CPR
  - 8% survived to hospital discharge
  - 3% alive at 6 months
  - ~80% died a mean of 4 days later, intubated in ICU

- Lai 1999: intradialytic CPR in 24 patients over 3 years
  - 75% were initially resuscitated successfully
  - 45% survived > 24 hrs
  - 8% survived > 1 month
  - None survived until discharge

- Lafrance 2006: intradialytic CPR in 24 patients over 7 years
  - 17% died within 48 hr
  - 75% were alive at 30 days and discharged from hospital
Theoretical Trajectories of Dying

Symptom Burden in Dialysis Patients
n = 507

Davison, et al. KI 2006;69:1621
## Severity of Pain: Brief Pain Inventory Scores

<table>
<thead>
<tr>
<th>Severity (n=103)</th>
<th>Mild (0-3)</th>
<th>Moderate (4-5)</th>
<th>Severe (6-10)</th>
<th>Mean BPI Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worst</td>
<td>17.5%</td>
<td><strong>82.5%</strong></td>
<td></td>
<td>7.03</td>
</tr>
<tr>
<td>Least</td>
<td>74.8%</td>
<td>16.5%</td>
<td><strong>8.7%</strong></td>
<td>3.07</td>
</tr>
<tr>
<td>Average</td>
<td>41.7%</td>
<td><strong>58.3%</strong></td>
<td></td>
<td>5.61</td>
</tr>
<tr>
<td>Now</td>
<td>44.7%</td>
<td>28.2%</td>
<td><strong>27.2%</strong></td>
<td>4.99</td>
</tr>
</tbody>
</table>

Cause of pain is NOT predictive for severity of pain

Davison, AJKD 2003
The Impact of Pain and Overall Symptom Burden for ESRD Patients

<table>
<thead>
<tr>
<th></th>
<th>No – Mild pain</th>
<th>Mod – Severe pain</th>
<th>Odds Ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>18%</td>
<td>34%</td>
<td>2.31</td>
<td>0.01</td>
</tr>
<tr>
<td>Insomnia</td>
<td>53%</td>
<td>75%</td>
<td>2.32</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Symptom burden accounted for **29%** of the impairment in physical HRQL and **39%** of the impairment in mental HRQL.

Change in symptom burden accounted for **34%** of the change in physical HRQL and **46%** of the change in mental HRQL.
### Point Prevalence of Analgesic Use: DOPPS

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1997 N = 2988</td>
</tr>
<tr>
<td>Any analgesic</td>
<td>30.2%</td>
</tr>
<tr>
<td>Any narcotic</td>
<td>18.0%</td>
</tr>
<tr>
<td>Any NSAID</td>
<td>6.4%</td>
</tr>
<tr>
<td>Any acetaminophen</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

¾ of patients reporting moderate to severe pain were not prescribed analgesics
Successes

- Identification of the problem
- Ethical guideline development
- Formation of frameworks to integrate renal palliative care
- Advances in prognosis estimation
- Advance care planning
- Pain and symptom assessment and management
Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

rpa@renalmd.org
301.468.3515
RPA Guideline Recommendations

1: Shared Decision-Making
2: Informed Consent or Refusal
3: Estimating Prognosis
4: Conflict Resolution
5: Advance Directives
6: Withholding or Withdrawing Dialysis
7: Special Patient Groups
8: Time-Limited Trials
9: Palliative Care
### Table 2. Comparisons of characteristics of nephrologists according to level of preparedness

<table>
<thead>
<tr>
<th>Characteristic of Nephrologists</th>
<th>Very Well Prepared (n = 143)</th>
<th>Less than Very Well Prepared (n = 211)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year fellowship completed</td>
<td>1985 ± 11</td>
<td>1992 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20 to 45</td>
<td>27</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>46 to 65</td>
<td>64</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>66+</td>
<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>No. of patients cared for</td>
<td>114 ± 83</td>
<td>109 ± 122</td>
<td>0.033</td>
</tr>
<tr>
<td>No. of patients who stopped dialysis in past year</td>
<td>5.6 ± 5.1</td>
<td>3.8 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use time-limited trials of dialysis</td>
<td>87</td>
<td>74</td>
<td>0.003</td>
</tr>
<tr>
<td>No. of patients referred to hospice in past year</td>
<td>3.9 ± 4.1</td>
<td>3.3 ± 3.9</td>
<td>0.039</td>
</tr>
<tr>
<td>Practice in units that refer patients to hospice</td>
<td>8/6</td>
<td>7/6</td>
<td>0.013</td>
</tr>
<tr>
<td>Medical school affiliation</td>
<td>52</td>
<td>54</td>
<td>0.644</td>
</tr>
<tr>
<td>Country of practice, United States</td>
<td>87</td>
<td>80</td>
<td>0.075</td>
</tr>
<tr>
<td>Unit policy on withdrawal of dialysis</td>
<td>31</td>
<td>22</td>
<td>0.062</td>
</tr>
<tr>
<td>Unit policy on CPR</td>
<td>80</td>
<td>79</td>
<td>0.812</td>
</tr>
<tr>
<td>Practice in units in which CPR is discussed routinely</td>
<td>93</td>
<td>85</td>
<td>0.029</td>
</tr>
<tr>
<td>Likely to consult an ESRD Network Ethics Committee for difficult patient treatment decisions</td>
<td>40</td>
<td>57</td>
<td>0.002</td>
</tr>
<tr>
<td>Aware of RPA/ASN guidelines</td>
<td>70</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use RPA/ASN guidelines&lt;sup&gt;a&lt;/sup&gt;</td>
<td>58</td>
<td>48</td>
<td>0.155</td>
</tr>
<tr>
<td>Aware of RPA/ASN statement</td>
<td>62</td>
<td>48</td>
<td>0.007</td>
</tr>
<tr>
<td>Use RPA/ASN statement&lt;sup&gt;a&lt;/sup&gt;</td>
<td>59</td>
<td>55</td>
<td>0.613</td>
</tr>
</tbody>
</table>

<sup>a</sup>Numbers and percentages are based on nephrologists who are aware of guidelines/statement.

Establishing a Palliative Care Framework for Advanced CKD

**Patient Identification**
- High mortality risk
- High need
  - Suffering
  - Goals of care
    (initiation or withdrawal of dialysis)

**Advance Care Planning**
- Surrogate decision-maker
- Goals of care
- Decision making

**Management of Suffering**
- Physical
- Emotional/psychosocial
- Spiritual
- Anticipatory grief

**Assess**

**Death**

**Bereavement**
Predictors of Poor Prognosis for ESRD Patients

- Age
- Nutritional status
  - Serum albumin < 35g/L
  - ~ 50% mortality at 1 year
  - 17% at 2 years
- Comorbid Illnesses – Charlson Comorbidity Index
  - CCI ≥ 8 ~ 50% 1 year mortality
- Surprise Question
- Functional Status

## Comorbidity Index and Score of Charlson et al

**Purpose:** To use the comorbidity score developed by Charlson et al to give an estimate of 10 year survival for a patient.

<table>
<thead>
<tr>
<th>Condition</th>
<th>None</th>
<th>Without and organ damage</th>
<th>With end organ damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Cerebrovascular disease?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Chronic pulmonary disease?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Congestive heart failure?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Connective tissue disease?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Dementia?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Hemiplegia?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Leukemia?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Malignant lymphoma?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Myocardial infarction?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Peripheral vascular disease?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
<tr>
<td>Ulcer disease?</td>
<td>![Yes]</td>
<td>![None]</td>
<td>![None]</td>
</tr>
</tbody>
</table>

Click the appropriate column for each condition (give only 1 answer per row).

**Calculate**  **Reset**
Would you be surprised if the patient died in the next year?

The surprise question helps identify patients for whom palliative care is appropriate:

The odds of dying (within 1 year) for the patients in the “No, I would not be surprised” group were 3.5 times higher than for patients in the “Yes, I would be surprised” group

- Mortality at 1 year = 29.4% v. 10.6%; OR 3.5
- Higher pain levels
- Greater comorbidity – Charlson Comorbidity Index
- Greater functional impairment – Karnofsky
- Older age
- Lower serum albumin

Survival by Surprise Question Response

Mean Days Alive
“Yes” = 356.0 ± 2.8
“No” = 328.4 ± 13.1
P = 0.005

No. at Risk
“Yes” 113 113 113 113 113 111 104 102 101
“No” 34 33 32 32 32 30 28 24 24
Survival by Comorbidity Score

Mean Days Alive
“CCI<8” = 357.4±2.6
“CCI≥8” = 344.0±6.4
P = 0.006

No. at Risk
CCI<8  102  101  95  93  93
CCI≥8  42   39  36  32  31
Incident pts > 75 yrs: predict early (< 6 month) mortality

- Demographics,
- Comorbidity
  - Diabetes, CHF (III/IV), PVD (III/IV), Dysrythmia
  - BMI < 18.5
  - Malignancy (active)
  - Severe behavioral disorder
- Mobility: totally dependent for transfers
- Unplanned dialysis start
- Point score
  - NDT 2008
# A New Integrated Model

## Table 5: Analysis of Maximum Likelihood Estimates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Explanation of units for the Hazard Ratio (HR)</th>
<th>DF</th>
<th>Parameter Estimate</th>
<th>Standard Error</th>
<th>Chi-Square</th>
<th>Pr &gt; ChiSq</th>
<th>Hazard Ratio</th>
<th>95% Hazard Ratio Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>HR per 1 unit increase</td>
<td>1</td>
<td>-1.26803</td>
<td>0.30031</td>
<td>18.025</td>
<td>&lt;0.0001</td>
<td>6.274</td>
<td>0.152</td>
</tr>
<tr>
<td>Surprise Question</td>
<td>HR - not surprised vs. surprised</td>
<td></td>
<td>0.99802</td>
<td>0.22004</td>
<td>20.4898</td>
<td>&lt;0.0001</td>
<td>2.787</td>
<td>1.759</td>
</tr>
<tr>
<td>Calcage</td>
<td>HR = per 1 year increase in age</td>
<td>1</td>
<td>0.03068</td>
<td>0.00755</td>
<td>17.4291</td>
<td>&lt;0.0001</td>
<td>1.357</td>
<td>1.17</td>
</tr>
<tr>
<td>Admentia_cclipt</td>
<td>HR: Dementia vs. not</td>
<td>1</td>
<td>0.80421</td>
<td>0.35389</td>
<td>5.1646</td>
<td>0.0231</td>
<td>2.235</td>
<td>1.117</td>
</tr>
<tr>
<td>Apvld_cclipt</td>
<td>HR: Periph Vasc Dis</td>
<td>1</td>
<td>0.83072</td>
<td>0.20104</td>
<td>9.0776</td>
<td>0.0026</td>
<td>2.879</td>
<td>1.047</td>
</tr>
</tbody>
</table>

## Baseline Survival

<table>
<thead>
<tr>
<th>TIME</th>
<th>6 month</th>
<th>12 month</th>
<th>18 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sq(t)</td>
<td>0.57921</td>
<td>0.24969</td>
<td>0.09187</td>
</tr>
</tbody>
</table>

## Predicted survival at time ‘t' = [Sq(t)]_{step (beta)}

**VARIABLE**

- Albumin (enter raw albumin level): 3.5 (if <2.5, enter 2.5; if >4, enter 4)
- SQ (enter 1 if not surprised, 0 if surprised): 1
- Age (enter actual age): 65
- Dementia (1=yes, 0=no): 0
- Periph Vascular Disease (1=yes, 0=no): 0

**NOTE:** age range for model development was 16-92; albumin range was 1.7 to 5

**RESULTS**

- Weighted value (param estimate*value): -4.536105
- X.BETA (pred.index): -1.546885
- Predicted 6mo survival: 89.0%
- Predicted 12mo survival: 74.4%
- Predicted 18mo survival: 60.1%

**SUM OF ALL OF STEP 3 (WEIGHTED VALUES - X.BETA)**

**PARAMETER (step 1)*COVARIATE (step 2)**

**THESE ARE THE PREDICTIONS... YOU CAN BACKTRACK THE FORMULA, THEY ARE CALCULATED AS THE CONSTANT (CELL E6-G12, DEPENDING ON TIME FRAME) RAISED TO THE (step 4) VALUE IN CELL L15 (aka X.BETA or PREDICTIVE INDEX)**

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Germain, Moss and Cohen. CJASN in press
Remaining Challenges: determining who will benefit from conservative management v. dialysis

- Pts > 75 yrs, eGFR < 15 ml/min
- Conservatively managed patients: older (83.0 v. 79.6);

<table>
<thead>
<tr>
<th></th>
<th>Dialysis (n = 52)</th>
<th>Conservative (n = 77)</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year survival</td>
<td>84%</td>
<td>68%</td>
<td>74%</td>
</tr>
<tr>
<td>2 year survival</td>
<td>76%</td>
<td>47%</td>
<td>58%</td>
</tr>
</tbody>
</table>

“…. survival advantage [for dialyzed patients] was lost in those patients with high comorbidity scores, especially when the comorbidity included ischaemic heart disease.”
Survival in elderly patients with CKD stage 5

Fig. 3. Kaplan-Meier survival curves for those with high comorbidity (score 2), comparing dialysis and conservative groups (log rank statistic < 0.001, df 1, P = 0.98).

Fig. 4. (A) Kaplan-Meier survival curves for those with ischemic heart disease, comparing the dialysis and conservative groups (log rank statistic 1.46, df 1, P = 0.27). (B) Kaplan-Meier survival curves for those without ischemic heart disease, comparing the dialysis and conservative groups (log rank statistic 12.78, df 1, P < 0.0001).
Functional Status of Elderly Adults before and after Initiation of Dialysis


**Figure 3.** Smoothed Trajectory of Functional Status before and after the Initiation of Dialysis and Cumulative Mortality Rate.

The dashed vertical line indicates the initiation of dialysis in a hypothetical 75-year-old nursing home resident. MDS–ADL denotes Minimum Data Set–Activities of Daily Living. The numbers on the MDS–ADL axis run from highest to lowest.
Advance Care Planning

- A process that involves understanding, reflection, communication and discussion between a patient, the family/health care proxy, and staff for the purpose of prospectively identifying a surrogate, clarifying preferences, and developing individualized plans for care near the end of life.

The focus is not merely death and the right to refuse treatment but rather about living well and defining “good care” for each patient near the end of life.
Goals of Care and ACP

“Goals of care are inextricably linked with patient and family understanding of illness and expectations. In the context of facilitated ACP, it is clear that goals must reflect expectations that are in balance with adequate knowledge.”

This includes prognostic information.

Patients' Desires for Treatments in Various Health States (%)

Talking About Prognosis & EOL Issues

“Yikes! Okay, I’m going to pretend I didn’t see that.”
Nephrologists should voluntarily divulge survival data to potential dialysis patients.

- 100 non dialysis CKD pts during 1st nephrology visit
- 97% want prognostic info without the MD being asked (only 3% did not want to know life expectancy with and without dialysis)
- They want as much info both good and bad
- Only 11% said that they did not need to know prognosis to make a decision on whether to start dialysis
Information-Giving within ACP Enhances Hope

- **Less fear**: early information, especially prior to RRT
- **Empowerment**
- **Enhanced relationships**
- **Type of information:**
  - Impact on daily life
  - Helps patients see future possibilities consistent with their values – essential in maintaining hope
- **Giving “bad prognostic” information does not result in harm and can have positive outcomes**

Davison, BMJ 2006
Conclusion: Most surrogates of critically ill patients do not view withholding prognostic information as an acceptable way to maintain hope, largely because timely discussions about prognosis help families begin to prepare emotionally, existentially, and practically for the possibility that a patient will die.
**Conclusions** End-of-life discussions are associated with less aggressive medical care near death and earlier hospice referrals. Aggressive care is associated with worse patient quality of life and worse bereavement adjustment.

**Figure.** Relationship Between Quality of Life and End-of-Life Care

Results are adjusted for illness severity, as measured by Kamofsky score and survival. Caregivers were asked, “In your opinion, how would you rate the overall quality of the patient’s death or last week of life?” Response items were arranged on a Likert scale from 0 “worst possible” to 10 “best possible.” The hospice statistical scores were $F=4.04_{2}, P<.001$. Interventions included ventilation, resuscitation, chemotherapy, or feeding tube ($F=3.61_{2}, P=.01$). Error bars represent 95% confidence intervals.
Key Elements to Facilitate Effective ACP

Davison CJASN 2007, AJKD 2007

**Patient participation**
1. Determine the patient’s *ability* to be involved in ACP
2. Determine the patient’s *interest* in participating in ACP
3. Determine the patient’s *perception* of level of control and power
4. Determine the patient’s *perception of potential benefits* of participation in ACP
5. Determine the patient’s *resources* to participate in ACP
6. Identify *whom* the patient wishes to engage in ACP

**Decision-making and defining priorities for goals of care**
1. Measure *understanding* of illness
2. Determine *how* patients expect to make decisions
3. Determine *expectations* regarding outcomes of end-of-life care
4. Determine patient *values* that drive end-of-life preferences
Key Elements to Facilitate Effective ACP

Patient-physician relationship
1. Use of lay language to promote understanding
2. Empathetic listening
3. Affirm patients’ self-worth
4. Maintain trust, honesty, promise keeping, confidentiality, and caring

Documentation
1. Easily identifiable
2. Travel with the patient across health care settings so it is available for all professional caregivers involved in the care of the patient.

Quality improvement

Supportive Care …..in press 2010
My Voice – Planning Ahead

fraserhealth
Better health. Best in health care

http://www.fraserhealth.ca/your_care/planning_for_your_care/workbook

www.calgaryhealthregion.ca/programs/advancecareplanning/acpgcdpolicy
Additional Challenges to be Faced

- Facilitation
  - Consensus on when to start discussions, who to include

- Systematic Integration
  - Providing the necessary resources: including reimbursement for the time involved

- Professional Training
  - Respecting choices

- Cultural differences that influence ACP
  - Concept of autonomy
  - Decision-making models
  - Communication of bad news
  - Attitudes towards ACP and end-of-life care

- Increase the uptake / effectiveness of ACP

Davison Adv Chronic Kidney Dis 2008
Interventions to Increase Uptake and Effectiveness of ACP

- **Written material on ADs** does not alter attitudes to ADs; only transiently improves understanding of end-of-life care issues.  
  Holley AJKD 2003

- **Peer mentoring**: RCT of 203 dialysis patients - increased completion of ADs, increased comfort discussing ADs, improved subjective wellbeing among the African American participants.  
  Perry AJKD 2005

- **Multi-component approaches “Respecting Choices”**
  - AD completion increased from 15% to 85%  
  - Median time between AD and death was 1.2 years.  
  - Almost all ADs requested that treatment be forgone as death neared and treatment followed these instructions in 98% of cases  
**Behavioural Change**

- **Health Information Technology**
  - Identify at risk patients
  - Provide automated reminders for ACP
  - ~8-fold increase in having an AD discussion with 45% of these discussions resulting in the completion of an AD.
  - Automated ACP reminder & mail out of educational material on ADs to patients prior to appointment. more ACP discussions (64% v. 38%, p<0.001) and more documentation of these discussions (47% v. 24%, p<0.001).
  - Share information across providers with a uniform instrument.
  - Promote adherence to guide-line based care.

- **Social Marketing**
  - “Respecting Choices”

- **Legislative & Policy Change**
  - POLST (Physicians Orders for Life Sustaining Treatment)
Successes

- Identification of the problem
- Ethical guideline development
- Formation of frameworks to integrate renal palliative care
- Advances in prognosis estimation
- Advance care planning
- Pain and symptom assessment and management
Initial Symptom Screening - ESAS

Edmonton Symptom Assessment System: Numerical Scale
Northern Alberta Renal Program

Please circle the number that best describes:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td></td>
<td>0-10 Worst possible pain</td>
</tr>
<tr>
<td>Not tired</td>
<td></td>
<td>0-10 Worst possible tiredness</td>
</tr>
<tr>
<td>Not nauseated</td>
<td></td>
<td>0-10 Worst possible nausea</td>
</tr>
<tr>
<td>Not depressed</td>
<td></td>
<td>0-10 Worst possible depression</td>
</tr>
<tr>
<td>Not anxious</td>
<td></td>
<td>0-10 Worst possible anxiety</td>
</tr>
<tr>
<td>Not drowsy</td>
<td></td>
<td>0-10 Worst possible drowsiness</td>
</tr>
<tr>
<td>Best appetite</td>
<td></td>
<td>0-10 Worst possible appetite</td>
</tr>
<tr>
<td>Best feeling of wellbeing</td>
<td></td>
<td>0-10 Worst possible feeling of wellbeing</td>
</tr>
<tr>
<td>No itching</td>
<td></td>
<td>0-10 Worst possible itching</td>
</tr>
<tr>
<td>No shortness of breath</td>
<td></td>
<td>0-10 Worst possible shortness of breath</td>
</tr>
<tr>
<td>Other problem</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient’s Name ___________________________  Complete by (check one)
Date ___________________ Time ___________________

- Onset
- Location
- Character
- Duration
- Intensity
- Severity – impact on HRQL
- Temporal characteristics
- Triggering/relieving factors
- Type (nociceptive, neuropathic)
- Psychologic symptoms
- Treatment (duration, dosage, side-effects)
- Goals & expectations of treatment

BODY DIAGRAM ON REVERSE SIDE
Below is a list of symptoms, which you may or may not have experienced. Please put a tick in the box to show how each of these symptoms has affected how you have been feeling over the last 3 days.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not at all, no effect</th>
<th>Slightly – but not bothered to be rid of it</th>
<th>Moderately – limits some activity or concentration</th>
<th>Severely – activities or concentration markedly affected</th>
<th>Overwhelmingly – unable to think of anything else</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathlessness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiredness or lack of energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea (feeling like you going to be sick)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting (being sick)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of appetite</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of mobility</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiffness legs or difficulty ping legs still</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling anxious</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling depressed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in skin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diarrhoea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Non-opioid ± adjuvant
Weak opioid for mild to moderate pain ± non-opioid ± adjuvant
Opioid for moderate to severe pain ± non-opioid ± adjuvant
Freedom from pain
Pain persisting or increasing
Non-opioid ± adjuvant
Pain persisting or increasing
Pain
Efficacy of the WHO Analgesic Ladder to Treat Pain in ESRD

<table>
<thead>
<tr>
<th>Type of Pain</th>
<th>Initial Pain Score (0-10)</th>
<th>Post Treatment Pain Score (0-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathic Pain</td>
<td>7.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Nociceptive Pain</td>
<td>7.5</td>
<td>1.8</td>
</tr>
</tbody>
</table>

45 HD patients

Barakzoy, JASN 2006
Clinical Algorithm & Preferred Medications to Treat Pain in Dialysis Patients

MARC
Developed by the Mid-Atlantic Renal Coalition and the Kidney End-of-Life Coalition
September 2009

This project was supported, in part, under CMS Contract #HHSM 500-2006-NW005C. The contents of this document do not necessarily reflect CMS policy.

OVERVIEW OF ESSENTIALS OF PAIN MANAGEMENT

- Assess pain intensity on a 0-10 scale in which 0 = no pain at all and 10 = the worst pain imaginable. Determine if the pain is mild (1-4), moderate (5-6), or severe (7-10).
- Prescribe pain medications and dosages according to the World Health Organization 3-Step Analgesic Ladder adapted for patients with chronic kidney disease (see page 2).
- Assess the character of the patient’s pain and determine whether it is nociceptive, neuropathic, or both. Patients may have more than one type of pain; each pain syndrome should be diagnosed and treated.
- Nociceptive pain involves intact pain receptors and is described by patients as aching, dull, throbbing, cramping, or pressure. Neuropathic pain involves injury to pain receptors and is described by patients as tingling, burning, stabbing, or numb (see pages 3 & 4). Treatment of severe neuropathic pain usually requires opioid medications in addition to gabapentin or pregabalin, or other medications specific for neuropathic pain.
- Assess pain regularly for site, relieving and aggravating factors, and temporal relationships, and assess treatment regularly for effect on functioning and quality of life.
- Believe the patient’s report of pain.
- Refer for non-pharmacological interventions as appropriate.
- Use adjuvant medications to reduce pain and side effects.
- Anticipate and treat constipation.
- Always consider depression as a potential contributor.
- Screen for opioid abuse.

RECOMMENDED PRACTICES

A Educate patient/caregivers on pain assessment and charting at home, goals of therapy, management plan, and potential complications.

B Aim to achieve control at a level acceptable to the patient; it may not be necessary or possible to make the patient completely pain-free. Provide p.r.n. doses for breakthrough pain.

C For chronic pain, schedule doses over 24 hours on a regular basis. Additional “breakthrough” medication should be available on an “as needed” basis.
**Analgesic Ladder**

**WHO 3-Step Analgesic Ladder**

**Severe Pain (7-10)**
- Hydromorphone – start at 1 mg PO q 4h, then 1 mg prn for breakthrough pain q 2h

**Moderate Pain (5-6)**
- Hydrocodone – start at 5 mg po q 4h prn
- Oxycodone – start at 5 mg po q 4h prn
- Tramadol – start at 25 mg po q d
- ± Nonopioid analgesics ± Adjuvants

**Mild Pain (1-4)**
- Acetaminophen
- Avoid NSAIDS
- ± Adjuvants

Do not exceed 4g of the acetaminophene per day to avoid hepatotoxicity.

Adjuvants include medications such as anticonvulsants for neuropathic pain. It may also refer to medications that are administered to manage adverse effects of an opioid or to enhance analgesia, such as steroids for pain from bone metastases.
ALGORITHM TO TREAT SEVERE CHRONIC PAIN IN DIALYSIS PATIENTS

Hydromorphone:
- Start at 0.5 - 1 mg PO q 4 hours plus 1 mg PO q 2 hours prn pain. Titrate dosage every 2 – 3 days.
- If pain is not controlled, is continuous, and 24-hour dose exceeds 12 mg, substitute transdermal fentanyl 25 mcg/h for regular dose of hydromorphone.
- If further “as needed” hydromorphone exceeds 12 mg/24 hours, increase dose of fentanyl patch by further 25 mcg. Titrate upwards in similar manner if pain is not controlled.
- Caution: Toxic metabolite, H3G, accumulates if dialysis is stopped.

Fentanyl Transdermal Patches:
- Useful for patients with chronic, stable pain. Start after immediate-release opioid dose is established. Analgesia may not be obtained for 12-24 hours, so continue previous prn analgesics for 12 hours to ensure a smooth transition.
- Initial dose for opioid-naïve patients is 12 mcg/h (increase dose every 3 – 6 days as needed for pain). Useful choice if dialysis non-adherence or stopping dialysis are concerns.
- Fentanyl patches above 12 mcg/hr should not be used in opioid-naïve patients due to risk of respiratory depression.
- Prescribe medication for breakthrough pain.

Methadone:
- Only recommended to be used by knowledgeable physicians.
- Use if unable to control pain with hydromorphone or fentanyl (opioid-allergy, adverse effects, or refractory pain).
- Obtain baseline QTc (methadone may prolong QT interval) and repeat EKG if daily dose > 100 mg. QTc < 450 ms considered safe.
- Beware of multiple drug interactions and adjust dose.
- Consult www.hopweb.org for opioid conversions from hydromorphone or fentanyl to methadone.
**NOCICEPTIVE PAIN TREATMENT**

*Note: Monitor for opioid toxicity (sedation, hallucinations, myoclonus and/or asterixis) and opioid adverse effects (constipation, nausea, and vomiting).*

- Confirm patient is able to swallow oral medications.
- Long-acting opioids should be started after the needed dosage to control pain is established with short-acting opioids.
- A rescue dose equivalent to 10% of the 24-hour dose of opioid should be available to be taken every 1-2 hours prn for breakthrough pain. Remember to recalculate the rescue dose when increasing the base dose (long-acting dose).
- If the patient is experiencing pain when he/she takes the long-acting opioid, he/she should take a rescue dose at the same time and not expect the long-acting opioid to relieve the breakthrough pain.

**NEUROPATHIC PAIN TREATMENT**

**Gabapentin:**
- Start 100 mg po q hs and increase weekly by 100 mg per night to a maximum of 300 mg q hs. Occasionally doses up to 600 mg a day can be safely used.
- If ineffective at maximum tolerated dose, discontinue and start Pregabalin.

**Pregabalin:**
- 25 mg q hs and increase every few days to 100 mg a day.
- If pain control is inadequate at target dose for 2 to 4 weeks, or intolerable adverse effects, discontinue and start Desipramine.

**Desipramine:**
- 10 mg po q hs. Titrate to adequate pain control or maximum dose of 150 mg q hs.
- If pain control still remains inadequate, institute WHO 3-Step Analgesic Ladder (see page 2).
MANAGEMENT OF OPIOID ADVERSE EFFECTS

Acute:
Excessive sedation, compromised respiration with low O2 saturation
- Dilute 0.4 mg of Naloxone in 10 ml NS and administer 1 ml IV q 1-2 minutes until patient arouses.
- Continue to monitor for return of sedation or slowed respirations (half-life of Naloxone is shorter than half-life of opioids).

Chronic:
Nausea and/or vomiting
- Prochlorperazine 2.5 to 10 mg PO, SC or PR QID prn.
- Haloperidol 0.5 to 1 mg PO, SL, SC, IV BID-TID prn (Haloperidol solution is flavorless).
- Metoclopramide 5 to 10 mg PO, SC, IV QID prn.
- Dimenhydrinate may be used 25 to 50 mg PO, SC, IV but is less effective except if secondary to motion/dizziness. It also reduces opioid-induced pruritus.
- Ondansetron 4-8 mg PO or IV q8H prn.

Constipation
- Start docusate sodium and stimulant laxative (e.g. Senna, Bisacodyl) at same time as opioids as preventative therapy.
- Lactulose at 15-30 ml po daily to BID is more effective for opioid-induced constipation but patients may prefer medication in pill form.

Cognitive impairment
- Try decreasing the opioid dose to determine if function improves. If it does, consider using a lower dose or a different pain medication.

References for this document can be found on the Kidney End-of-Life Coalition website: www.kidneyeol.org.
# Preferred Medications in CKD

## Recommended

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
</tr>
<tr>
<td>Methadone</td>
</tr>
<tr>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Gabapentin</td>
</tr>
</tbody>
</table>

- **Gabapentin**: Doses up to 300 mg/d are generally considered safe in ESRD, but doses up to 600 mg should be used with caution; note that gabapentin use for neuropathic pain is off-label but effectiveness has been documented.

## Use with Caution

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
</tr>
<tr>
<td>Hydrocodone/Oxycodone</td>
</tr>
</tbody>
</table>

- **Tramadol**: Limit dose to 30 mg BID. Higher doses have been used but caution needs to be taken since pharmacokinetics are not well established.

- **Hydrocodone/Oxycodone**: Insufficient pharmacokinetic evidence to establish safety in CKD, but literature reports use without major adverse effects.

## DO NOT USE

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
</tr>
<tr>
<td>Codeine</td>
</tr>
<tr>
<td>Meperidine</td>
</tr>
<tr>
<td>Propoxyphene</td>
</tr>
</tbody>
</table>

- **Morphine, codeine, meperidine, propoxyphene**: Renally excreted metabolites accumulate in CKD causing neurotoxicity.
**PAIN ASSESSMENT**

**Instructions:** Please have your patient describe his/her level of pain by circling the appropriate number or the face that best describes the intensity of pain. Determine if the pain is nociceptive or neuropathic by the descriptors the patient uses to describe the pain (see algorithm below). Repeat the pain assessment on subsequent patient visits.

1. “Are you having any pain?”
   - *Verbal:* “How much pain are you having, from 0 (no pain) to 10 (worst pain imaginable)?”
   - *Written:* “Circle the number that describes how much pain you are having.”

**NUMERICAL RATING SCALE**

<table>
<thead>
<tr>
<th>No pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Worst imaginable pain</th>
</tr>
</thead>
</table>

**CATEGORICAL SCALE/FACES R**

- None (0)
- Mild (1-4)
- Moderate (5-6)
- Severe (7-10)

2. “Where is the pain located?”
   Record, screen and address each site.

3. “How much pain are you having?”
   Use *Pain Screening Tool—Numerical Scare or Categorical Faces/R Scale* (for cognitively impaired).

4. “What is the character of the pain?”
   - Nociceptive—Patient descriptors: *aching, dull, throbbing, cramping, pressure*
   - Neuropathic—Patient descriptors: *tingling, numbness, burning, stabbing, increased pain to light touch*
   - Both Nociceptive and Neuropathic

5. “What relieves the pain?”, “What aggravates the pain?”
Remaining Challenges

- End-of-life care training for nephrology staff
End-of-life Care Training in Nephrology

Hemodialysis

Distal RTA

End-of-Life Care

0 = no teaching or completely unprepared  
10 = a lot of teaching or completely prepared
During your fellowship, were you explicitly taught to:

- Determine when to refer to hospice
- Respond to request to stop dialysis
- Help with reconciliation and goodbyes
- Assess and manage depression at eol
- Tell patient he/she is dying
- Treat pain

% fellows who received explicit teaching on topic
End-of-life Care Training in Nephrology

AJKD2003;42:813-820

Renal Biopsies Performed

- % fellow
- Biopsies Performed
- Biopsies Performed While Observed

Family Meetings Conducted

- % fellow
- Family Meetings Conducted
- Family Meetings Conducted While Observed

# biopsies performed

# family meetings performed
“There’s no easy way I can tell you this, so I’m sending you to someone who can.”
### Dialysis Withdrawal and Hospice Status of Deceased Patients: USRDS 2001-2002 Cohort

<table>
<thead>
<tr>
<th>Dialysis Withdrawal and Hospice Status</th>
<th>Deceased Patients (N=115,239)</th>
<th>Percent</th>
<th>Mean Age in Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice Yes</td>
<td>15,565</td>
<td>13.5</td>
<td>73.4 ± 11.0 *</td>
</tr>
<tr>
<td>Hospice No</td>
<td>99,674</td>
<td>86.5</td>
<td>68.6 ± 13.4</td>
</tr>
<tr>
<td>Withdrawal Yes</td>
<td>25,075</td>
<td>21.8</td>
<td>72.7 ± 11.8 **</td>
</tr>
<tr>
<td>Hospice Yes</td>
<td>10,518</td>
<td>41.9</td>
<td>73.9 ± 10.6</td>
</tr>
<tr>
<td>Hospice No</td>
<td>14,557</td>
<td>58.1</td>
<td>71.7 ± 12.3</td>
</tr>
<tr>
<td>Withdrawal No</td>
<td>81,624</td>
<td>70.8</td>
<td>68.0 ± 13.4</td>
</tr>
<tr>
<td>Hospice Yes</td>
<td>2,751</td>
<td>3.4</td>
<td>71.7 ± 11.7</td>
</tr>
<tr>
<td>Hospice No</td>
<td>78,873</td>
<td>96.6</td>
<td>67.9 ± 13.5</td>
</tr>
<tr>
<td>Withdrawal Status Unknown</td>
<td>8,540</td>
<td>7.4</td>
<td>71.1 ± 13.2</td>
</tr>
</tbody>
</table>

*Murray and Moss, CJASN 2006*
Figure 1. Americans’ Current Health Care Expenditures Are Concentrated in the Final Part of the Life Span

Gray area under the curve equals 100% of all health care expenditures over a life span

RAND Health White Paper, Living Well at the End of Life, 2006
## Costs Associated with Hospice Use in ESRD: USRDS 2001-2002 Cohort

<table>
<thead>
<tr>
<th>Dialysis Withdrawal and Hospice Status</th>
<th>Patients (N)</th>
<th>Mean cost last 6 months of life (US$)</th>
<th>Mean cost last week of life (US$)</th>
<th>Mean hospital days last week</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 month cohort</td>
<td>91,687</td>
<td>64,461</td>
<td>6,885</td>
<td>3.0</td>
</tr>
<tr>
<td>Patients who withdrew</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice Yes</td>
<td>8,200</td>
<td>60,261</td>
<td>3,324</td>
<td>1.4</td>
</tr>
<tr>
<td>Hospice No</td>
<td>11,317</td>
<td>66,253</td>
<td>6,257</td>
<td>3.7</td>
</tr>
<tr>
<td>Withdrawal No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice Yes</td>
<td>2,165</td>
<td>64,979</td>
<td>4,318</td>
<td>1.8</td>
</tr>
<tr>
<td>Hospice No</td>
<td>65,868</td>
<td>65,345</td>
<td>7,588</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Murray and Moss, CJASN 2006
### Site of Death and Hospice Days: USRDS 2001-2002 Cohort

<table>
<thead>
<tr>
<th>Dialysis Withdrawal and Hospice Status</th>
<th>Site of Death</th>
<th>Site of Death (%)</th>
<th>Mean days in Hospice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Home</td>
<td>Hospital Home</td>
<td>63.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Hospital Home</td>
<td>Home</td>
<td>16.7</td>
<td></td>
</tr>
</tbody>
</table>

**Patients who withdrew**

<table>
<thead>
<tr>
<th>Hospice Yes</th>
<th>Hospital Home</th>
<th>22.5</th>
<th>10.1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Home</td>
<td>45.3</td>
<td></td>
</tr>
<tr>
<td>Hospice No</td>
<td>Hospital Home</td>
<td>68.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Home</td>
<td>10.8</td>
<td></td>
</tr>
</tbody>
</table>

**Withdrawal No**

<table>
<thead>
<tr>
<th>Hospice Yes</th>
<th>Hospital Home</th>
<th>41.8</th>
<th>21.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Home</td>
<td>37.3</td>
<td></td>
</tr>
<tr>
<td>Hospice No</td>
<td>Home</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Murray and Moss, CJASN 2006
Remaining Challenges

- Enhance pain & symptom management & HRQL
- Enhance management of other symptoms, including spiritual distress
- Fully integrate advance care planning
- Identify which patients would benefit from a palliative care (conservative) as opposed to dialytic approach to their ESRD
- Increase access to palliative care including hospice for dialysis patients