Renal Palliative Care – An Overview

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South Australian Palliative Care Association – Annual Conference, Adelaide, May 2015.
A 53 year old woman

- Type 2 Diabetes Mellitus
- Hypertension
- OA – mild
- ESKD – Diabetic Nephropathy
- HD 3/week for 5 years
• Shuffled in to the clinic room

• Head down

• No eye contact
“My legs move all through the night” – Severe Restless Legs Syndrome - 2 years
“I itch all the time… often it becomes ferocious”
Severe uraemic pruritus – 3 years
“My feet and calves burn and get pins and needles – it is awful”

Severe diabetic peripheral neuropathy – 18 months
And sleep?
“I don’t sleep… I doze in 5 minute lots…

“I sit on a chair and put my elbows on my knees to hold them still…

and I pray to die.”
Overview

What role does Palliative Care have in Nephrology?
Withholding and withdrawing from dialysis
What exactly is the conservative, non-dialytic management of ESKD?
Symptom management
Care of the dying patient with ESKD
Creating and nurturing a Renal Supportive Care service
What possible role does Palliative Care play in End Stage Kidney Disease?
1. Epidemiology
DIALYSIS PATIENTS

In developed nations the characteristics of patients on dialysis have changed over the years.

Essentially more elderly patients with co-morbidities.
Number Starting Renal Replacement Therapy
Dialysis or Transplantation
Australia and New Zealand

Year

New Patients, Australia
0 500 1000 1500 2000 2500

New Patients, NZ
0 500 1000 1500 2000 2500

New Patients, Australia
Australia - New Zealand

New Patients, NZ
New Zealand
In Australia the mean age of patients commencing RRT is 60 years.

ANZDATA Annual Report 2014.
The age cohort that has the greatest prevalence on dialysis is the 65-84 year old group.

ANZDATA Annual Report 2014.
Does everyone who has ESKD commence dialysis?
In Australia, for every one patient with ESKD receiving Renal Replacement Therapy (RRT) there is another who does not receive RRT

Australian Institute of Health and Welfare Research, 2011
2. Mortality
ESRD patients

Overall patients with ESKD with or without RRT have a reduced life expectancy compared to age-matched controls.
DIALYSIS

For patients on dialysis 13.7 % die each year (ANZDATA 2014 Report)
For those aged 75 years and older that figure is 25 %
3. Symptomatology
“Patients with CKD, particularly those with ESRD are among the most symptomatic of any chronic disease group.”

What are the common symptoms associated with ESKD?
The Prevalence of Symptoms in End-stage Renal Disease: A systematic Review

Murtagh FE et al. *Advances in Chronic Kidney Disease* Vol 14, No 1 (January) 2007; pp 82-99
A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dialysis</th>
<th>Conservative</th>
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<tbody>
<tr>
<td>FATIGUE/TIREDNESS</td>
<td>71%</td>
<td>75%</td>
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<tr>
<td>PRURITUS</td>
<td>55%</td>
<td>74%</td>
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<tr>
<td>CONSTIPATION</td>
<td>53%</td>
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<tr>
<td>ANOREXIA</td>
<td>49%</td>
<td>47%</td>
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<tr>
<td>PAIN</td>
<td>47%</td>
<td>53%</td>
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<tr>
<td>SLEEP DISTURBANCE</td>
<td>44%</td>
<td>42%</td>
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# SYMPTOM PREVALENCE

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<tr>
<th>Symptom</th>
<th>Dialysis</th>
<th>Conservative</th>
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<td>Anxiety</td>
<td>38 %</td>
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<tr>
<td>Dyspnea</td>
<td>35 %</td>
<td>61 %</td>
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<tr>
<td>Nausea</td>
<td>33 %</td>
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<td>Restless Legs</td>
<td>30 %</td>
<td>48 %</td>
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<td>Depression</td>
<td>27 %</td>
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</table>
• Symptoms are prevalent

• Symptoms are multiple

• Symptoms are burdensome
4. Quality of life
QOL - St George dialysis (SF-36 Scores)

Mean score (max 100)

2001
2003
2004
2006
2008
Aust Norms

PF  RP  BP  GH  VT  SF  RE  MH
5. The “quality” of dying
Realistically, given issues of manpower, it may not be possible for a Palliative Care health professional to be present in every Renal Unit.
What are the core competencies in a “Palliative approach” to patients with ESKD for medical practitioners?
4 Pillars of a Palliative approach

- Communication
- Symptom management
- Psychosocial support
- Care of the dying patient
Communication
Once ESRD is diagnosed it is important to examine the various options.
RRT

Conservative
Decision making around dialysis
Survival
Dialysis or not? A comparative study of survival of patients over 75 years with CKD Stage 5.

Survival

[Graph showing cumulative survival over days after eGFR fell below 15 ml/min for Dialysis (n = 52) and Conservative (n = 77) groups.

Survival benefit lost if Co-morbidities include IHD

RRT v Conservative
Chandra et al, NDT Nov 2010

Graphs showing cumulative survival for Low comorbidity (p = 0.03) and High comorbidity (p = 0.83) comparing RRT and Conservative approaches.
Dialysis in Frail Elders — A Role for Palliative Care

Robert M. Arnold, M.D., and Mark L. Zeidel, M.D.
Change in Functional Status after Initiation of Dialysis

3702 Nursing home residents mean age 73
Mean eGFR 10
Female 60%
Diabetes 68%
CHF 66%
CHD 44%
Cerebrovascular dis. 39%
Depression 35%
Dementia 22%

Kurella Tamura et al. 361 (16): 1539, October 15, 2009
Smoothed Trajectory of Functional Status before and after the Initiation of Dialysis and Cumulative Mortality Rate

[Nursing home residents mean age 73]
Clinical Practice Guidelines on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

Renal Physicians Association of the USA 2010.
Recommendation No. 6

It is reasonable to consider forgoing dialysis for ... ESRD patients who have a very poor prognosis or for whom dialysis cannot be provided safely.
1. Those whose medical condition precludes the technical process of dialysis because the patient:

(a) is unable to co-operate (eg. Advanced Dementia)
(b) unstable medically (eg. Significant hypotension)
2. Another life-limiting illness – although this may be negotiated
3. Over 75 years
with 2 or more of the following statistically significant criteria predictive of very poor prognosis:

(a) Surprise question.
(b) High Co-morbidity Score
(c) Significantly impaired Functional status such as Karnofsky < 40,
(d) Severe chronic malnutrition (s. Albumin < 25.)
Conservative management of ESRD
This may be decided in consultation with a Nephrologist, or

The patient is not referred to a Nephrologist in the first place
What level of care occurs for this group?
If this is being raised as an option:

What does a Conservative pathway mean?

What is its content?

Can we make predictions about their course?
Challenge is to ensure that this pathway of management is not seen as “second best” or inadequate but is thorough, systematic and evidenced-based
Renal Medicine

Blood Pressure
Calcium/Phosphate
Anaemia
Fluid balance

Palliative approach

Symptom management
Psychosocial support
Care of the dying
There is a modest, but growing body of literature of research on this cohort of patients.
Longitudinal study of conservative stage 5 CKD

- Included patients with Stage 5 Chronic Kidney Disease with definite decision for conservative (non dialysis) management, and with capacity for consent
- 73 participants (response rate 62%)
- 49 (66%) died during follow-up
  - mean age 81 years, range 58-95 yrs
  - 24 (49%) men
  - median follow-up 8 months (range 1-23 months)
- Outcomes measured monthly until death or study end
  - Symptoms (MSAS-SF)
  - Palliative needs (POS)
  - Functional status (KPS)
Trajectory of functional status:

![Graph showing trajectory of functional status with time before death (months) on the x-axis and KPS (%) on the y-axis. The graph includes mean KPS and 95% confidence intervals.](www.kcl.ac.uk/palliative)
Trajectory of symptom distress:

**MSAS-Global Distress Index**
(0-100 scale)

![Graph showing trajectory of symptom distress index over time. The graph indicates an increase in distress closer to death, with a shaded area representing 95% confidence intervals.](image-url)
Trajectory of palliative needs:

Palliative outcome scale (0-100 scale)

- mean POS score
- 95% confidence intervals

Time before death (months)

n=10
n=43

www.kcl.ac.uk/palliative
Symptom management
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Symptom control is challenging
Symptoms interact and compound each other
Nocturnal:

U. Pruritus

RLS → Insomnia → Fatigue

Pain
Symptoms may derive from the co-morbidities
ESKD constrains the use of medication
Pharmacology in the context of CKD is complex with the altered pharmacokinetics of most medications in renal impairment.
Multiple gaps in knowledge
Recommendations in published data occasionally conflict on the specific doses of medications to be used.
Principles of symptom management

1. Think of the cause(s).

2. Be meticulous

3. Principle of non-abandonment
URAEMIC PRURITUS
Associations

- Poor sleep quality
- Depression
- QOL
- Mortality

The pathogenesis of pruritus
Complex neural network within the dermis and nerve fibres enter the Epidermis as free nerve endings
C Fibres
5 - 10 % of the C fibres are itch sensitive
For many years the assumption was:

Histamine $\rightarrow$ C Fibres $\rightarrow$ Spinal Cord
Of the C Fibres that are itch-sensitive:

20 % are Histamine-sensitive

80 % are Histamine-insensitive
Myth 1

That all itch is histamine mediated
Myth 2

That the best first line medication for pruritus of whatever cause are Anti-Histamines
Pathogenesis of Uraemic Pruritus
Multiple theories, conflicting findings
“Despite this vast array of possible explanations, none consistently have been demonstrated to be the underlying cause of pruritus associated with CKD. Large epidemiological studies ultimately may facilitate our understanding of the elusive pathophysiological process of this distressing symptom.”

Large number of therapies described
What therapies have the strongest foundation in evidence – based practice?
• Oral medications

• Topical preparations

• UV Therapy
Gabapentin
There are 3 (three) Level 1 studies showing that Gabapentin has significant efficacy in treating uraemic pruritis

Naini et al (2007)  
Razeghi et al (2009)
On Dialysis

Gabapentin 100mg after each Dialysis and titrating to effect
On conservative management with eGFR < 15

Gabapentin 100mg every second night and titrating to effect
On conservative management with eGFR > 15

Gabapentin 100mg nocte and titrating to effect
Evening Primrose Oil
Gabba Linolenic Acid (GLA)
Essential Fatty Acids (EFA) in the epidermis
n-6 EFA

Linolenic Acid (LA)

Gabba – Linolenic Acid (GLA)

DGLA

Arachidonic Acid

Adrenic Acid

Docosapentaenoic Acid
n-EFA

Linolenic Acid (LA)

↓

Gabba – Linolenic Acid (GLA)

↓

DGLA

↓

Arachidonic Acid (AA)

↓

Adrenic Acid

↓

Docosapentaenoic Acid

PGE2 ← Arachidonic Acid (AA)

Leukotriene B4 ← Adrenic Acid

Leukotriene B4 ← Docosapentaenoic Acid
n-6 EFA

Linolenic Acid (LA)
↓
Gabba-Linolenic Acid (GLA)
↓
PGE1 15-OH DGLA

DGLA
Arachidonic Acid (AA)
↓
Adrenic Acid
↓
Docosapentaenoic Acid
So supplementing the Gabba-Linolenic Acid (GLA) has an anti-inflammatory/anti-itch effect
100mg bd

= Evening Primrose Oil
contains GLA
= 1-2 capsules bd
Thalidomide  100mg nocte

Silva SR. *Nephron* 1994; 67(3): 270-273
Other oral medications

- Anti-Histamines – evidence does not support use.
- Ondansetron – conflicting results. Not recommended.
- Cimetidine – not recommended
- Naltrexone – conflicting results. Not recommended.

Murtagh FEM, Weisbord D. Symptom management in Renal Failure. In: Chambers EJ et al (eds). Supportive Care for the Renal Patient. 2nd ed. 2010. OUP. p. 120
Topical preparations
Moisturisers
Capsaicin cream (0.025 %)

Side effect – transient “burning” feeling on the skin
UV-B Therapy
Definition

1. An urge to move the limbs, usually associated with parasthesias/dysthesias
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.

Incidence in the general population: 2-15 %

Incidence in ESRD: 20-30 %
Mechanism is not completely understood
Fe

TH

Tyrosine → L-Dopa → Dopamine → DR2
Management

Clonazapem

0.5mg – 1mg nocte
Dopamine agonists
• Ergot-Dopamine Agonists (Pergolide, Cabergoline)

• Non-Ergot Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)
Gabapentin
Two Level 1 studies have shown efficacy for Gabapentin in the treatment of RLS in Dialysis patients

• Study A – Placebo controlled – Thorp et al (2001)

• Study B – Gabapentin compared to Levodopa – Micozkadioglu et al (2004)
A 53 year old woman

- Type 2 Diabetes Mellitus
- Hypertension
- OA – mild
- ESKD – Diabetic Nephropathy
- HD 3/week for 5 years
Referred to clinic because of extreme:

1. Uraemic Pruritus
2. Restless Legs Syndrome
3. Diabetic PN
3. Very poor sleep
Gabapentin
Gabapentin commenced for all conditions at 200mg at the completion of each dialysis.
• Complete cessation of all symptoms and a markedly improved sleep

• Sleeping “the best I have for a long time.”
Care of the dying patient with ESKD
ESKD patients may die:

- Having been on dialysis
- Never having been on dialysis
Patients with ESKD on dialysis may die in many different ways
The family’s view of the manner of dying and the care given will have a major effect on their bereavement and will echo down the years in the way they view death.
A major sentinel event → Sudden death
The “negotiated withdrawal”
• George has been on dialysis for 6 months

• He is increasingly fatigued and more frail. No clear reversible cause.

• Further exacerbations of Chronic Airways Limitation.
• NSTEMI

• He presents with a gangrenous toe - post amputation, worsening gangrene… discussion about further surgery.
“It’s time to talk to him and his family about the future. We need to be honest. It is right to say to him that he could withdraw from dialysis at any time, that would be OK. We would then speak about what to expect from that point onwards including our care for he and his family.”
Nephrologist 2

“If he brings it up of course I will talk to him...but only if he raises it. It should come from him.”
It is important that any discussion about withdrawal is open and honest at the patient’s own pace and includes the family.
• What should I expect?
• Will I suffer?
• Will I drown in fluids?
• How long will I live?
Patients survive a variable time.

- If completely anuric – 7-10 days
- If still passing urine – weeks-months
“A crisis withdrawal”
Scenario 1

The major sentinel event occurs …
• Family prepared for imminent death

• Dialysis ceased

• Consensus that there will not be an escalation to ICU etc.
Scenario 2

The major sentinel event occurs…
• No discussion about withdrawal

• Waiting approach

• Patient dies on dialysis, the day of dialysis
This scenario is considerably assisted if there the patient has had prior conversations with their Nephrologist including an Advance Care Plan
Creating and nurturing a Renal Supportive Care service
St George Hospital, Sydney, Australia

Collaboration between the departments of Renal Medicine and Palliative Medicine.
Formation of a Renal Supportive Care Clinic

March 2009
• Held every week

• Held in the Renal Unit

• Palliative Care Consultant, Advanced Trainee in Renal Medicine, Renal Supportive Care Nurse, Renal Social Worker, Renal Dietician
All patients with ESKD according to needs
Main categories of patients who are referred to the clinic:

• Patients who are on a conservative pathway

• Patients who need assistance in decision making around choosing dialysis or not

• Patients who are on dialysis and have cancer or other terminal conditions.
• Patients on dialysis who are experiencing symptoms which are difficult to manage

• Patients on dialysis who need assistance in decision making regarding withdrawing or continuing with dialysis
• Focus on symptom management

• Psychosocial support

• Preliminary discussions on ACP

• Access to Renal Social Worker and Renal Dietician
# Questionnaire POS-S (renal) – staff version

Below is a list of symptoms which the patient may or may not have experienced. Please record how these symptoms have affected the patient in the table below. Put a tick in the box to show how you think they have affected how they have been feeling **over the last week**.

<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 affects activities or concentration</th>
<th>Overwhelmingly unable to think of anything else</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td></td>
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<tr>
<td>Shortness of breath</td>
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<td>Weakness or lack of energy</td>
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<td>Nausea (feeling like you are going to be sick)</td>
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<tr>
<td>Vomiting (being sick)</td>
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<tr>
<td>Poor appetite</td>
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<tr>
<td>Constipation</td>
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<tr>
<td>Mouth problems</td>
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<tr>
<td>Drowsiness</td>
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<tr>
<td>Poor mobility</td>
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<tr>
<td>Itching</td>
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<td>Difficulty sleeping</td>
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<td>Restless legs or difficulty keeping legs still</td>
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<tr>
<td>Feeling anxious</td>
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<tr>
<td>Feeling depressed</td>
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<tr>
<td>Changes in skin</td>
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<tr>
<td>Diarrhoea</td>
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<td>Any other symptoms?</td>
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Which symptom has affected the patient the most? ........................................................................................................

Which symptom, if any, has improved the most? ........................................................................................................
Teaching programme for Junior Medical Staff, including Nephrology Trainees on all aspects of Renal-Supportive Care
Preparation of documents:

(a) End of Life Pathway for Renal Patients

(b) Commonly used Palliative medications in the context of CKD

(c) A Renal-Palliative Care Reader
Annual Renal Memorial Service
Annual Renal Palliative Care Symposium

2010 - 2014
Renal Supportive Care Curriculum

- Master Class for trainees 2015
What are the best books and materials in this area?
Chambers EJ, Germain M, Brown E (eds)  
*Supportive Care for the Renal Patient*  
2nd edition, 2010  
Oxford University Press
Clinical Practice Guideline on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis

Renal Physicians Association of the USA and the American Society of Nephrology. 2010.
Australasian Renal Supportive Care
Position Statement

Endorsed by Kidney Health Australia
Endorsed by the Australian and New Zealand Society of Nephrology

*Nephrology* 2013;18(6)
Davison SN et al.

Executive summary of the KDIGO Controversies Conference on Supportive Care in CKD: developing a roadmap to improving quality care.

*Kidney International*, Advance online publication, April 29 2015.
Conclusion

A mutual acknowledgement of need-

The role of Palliative Care/supportive care in ESRD
The last decade has seen considerable levels of advocacy, attitudinal shift, research, publications and collaboration
This approach may come at multiple points in the trajectory of the disease.
The core competencies in a “Palliative approach” to patients with ESKD can and should be acquired by all doctors working with these patients.
Applies to patients who are being managed either with dialysis or conservatively
The family will remember forever your involvement, your demeanour and your compassion
Your patients remain your patients until their death