Renal Supportive Care – An Overview

Frank Brennan
Palliative Care Consultant
Department of Nephrology
St George Hospital Sydney, Australia

Hospice New Zealand Palliative Care Lecture Series.
July 7 2016.
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

1. The disciplines of Nephrology and Palliative Care.
2. What possible role does Palliative Care have in Nephrology?

The interface of the two disciplines.
3. Core competencies in Renal Supportive care
4. Decision making around dialysis including the possible withholding and withdrawing from dialysis
5. What exactly is the conservative, non-dialytic management of ESKD?
6. Symptom management
7. Care of the dying patient with ESKD
1. The disciplines of Nephrology and Palliative Care.
Nephrology is the discipline that concentrates on the diagnosis and management of kidney diseases.

It includes the overseeing of Renal Replacement Therapy (RRT)
What is Palliative Care?
2. What possible role does Palliative Care have in Nephrology?

The interface of the two disciplines.
A. Epidemiology
Beginnings to the present
In Australasia 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.
The global epidemiology of Diabetic Nephropathy
The percentage of incident patients with ESKD that have diabetic nephropathy is:

> 50 % in Singapore, Malaysia, New Zealand

40 -50 % in Hong Kong, Taiwan, Republic of Korea, Japan and the USA.
The significantly disproportionate impact of Diabetes and diabetic nephropathy on the indigenous population.
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
B. Mortality
ESRD patients

Overall patients with ESKD with or without RRT have a reduced life expectancy compared to age-matched controls.
For patients on dialysis 13.7 % die each year (ANZDATA 2014 Report)
For those aged 75 years and older that figure is 25 %
C. Symptomatology
“Patients with CKD, particularly those with ESRD are among the most symptomatic of any chronic disease group.”

D. Quality of life
E. The “quality” of dying
Interface of Nephrology and Palliative Care

1. Epidemiology
2. Mortality
3. Morbidity
4. QOL
5. “Quality of dying”
3. Core competencies
in Renal Supportive Care
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 of clinicians in a “Palliative approach” to patients with ESKD?
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
3. Decision making around dialysis
Survival
Dialysis or not ? A comparative study of survival of patients over 75 years with CKD Stage 5.

Survival

Cumulative survival vs Days after eGFR fell below 15 ml/min

- Dialysis (n = 52)
- Conservative (n = 77)
Survival benefit lost if Co-morbidities include IHD

RRT v Conservative
Chandra et al NDT Nov 2010
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]
CKD in Elderly Patients Managed without Dialysis: Survival, Symptoms, and Quality of Life

Mark A. Brown,*† Gemma K. Collett,* Elizabeth A. Josland,* Celine Foote,‡ Qiang Li,‡ and Frank P. Brennan*
In patients over 75 years with 2 or more co-morbidities (one of which was IHD or CCF) there was no survival advantage with dialysis compared to those who did not commence dialysis.
One-third of non-dialysis patients lived more than 12 months after eGFR fell below 10ml/min
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 (e.g. Advanced Dementia)
(b) unstable medically (e.g. 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.)
5. What exactly is the conservative, non-dialytic management of ESKD?
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?
“What will happen to me if I don’t start Dialysis?”
Challenge is to ensure that this pathway of management is not seen as “second best” or inadequate but is thorough, systematic and evidenced-based
CKD conservative management

Not abandonment
CKD conservative management

Not simply transfer to Palliative Care
Renal Medicine

Blood Pressure
Calcium/Phosphate
Anaemia
Fluid balance

Palliative approach

Symptom management
Psychosocial support
Care of the dying
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:

- Mean KPS
- 95% confidence intervals

Time before death (months)

KPS (%)

n=10

n=43

www.kcl.ac.uk/palliative
Trajectory of symptom distress:

MSAS-Global Distress Index (0-100 scale)

Time before death (months)

n=10

n=43

mean MSAS-GDI

95% confidence intervals

www.kcl.ac.uk/palliative
Trajectory of palliative needs:

Palliative outcome scale
(0-100 scale)

Time before death (months)

- mean POS score
- 95% confidence intervals

n=10  
n=43
6. Symptom management
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

## SYMPTOM PREVALENCE

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dialysis</th>
<th>Conservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>FATIGUE/TIREDNESS</td>
<td>71%</td>
<td>75%</td>
</tr>
<tr>
<td>PRURITUS</td>
<td>55%</td>
<td>74%</td>
</tr>
<tr>
<td>CONSTIPATION</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>ANOREXIA</td>
<td>49%</td>
<td>47%</td>
</tr>
<tr>
<td>PAIN</td>
<td>47%</td>
<td>53%</td>
</tr>
<tr>
<td>SLEEP DISTURBANCE</td>
<td>44%</td>
<td>42%</td>
</tr>
<tr>
<td>ANXIETY</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>DYSPNEA</td>
<td>35%</td>
<td>61%</td>
</tr>
<tr>
<td>NAUSEA</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>RESTLESS LEGS</td>
<td>30%</td>
<td>48%</td>
</tr>
<tr>
<td>DEPRESSION</td>
<td>27%</td>
<td></td>
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</tbody>
</table>
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

• Restless Legs Syndrome

• Pain
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?
• Topical preparations

• Oral medications

• UV Therapy
Moisturisers
Capsaicin cream (0.025 %)

Side effect – transient “burning” feeling on the skin
Gabapentín
Gabapentin for uremic pruritus in hemodialysis patients: a qualitative systematic review.

“Our review supports a trial of Gabapentin for the management of UP in hemodialysis patients refractory to antihistamines and/or emollients. The results should be interpreted cautiously due to the lower quality of included studies. We recommend a starting dose of 100mg after hemodialysis to minimize adverse events…”
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
Pregabalin
Several prospective cohort studies showed efficacy.

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
- Leukotriene B4
n- 6 EFA

Linolenic Acid (LA)

↓

Gabba –Linolenic Acid (GLA)

↓

DGLA

PGE1

15 –OH 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
Sertraline (SSRI)

Shakiba M et al. *Int J Nephrology* 2012; Article ID 363901; 1-5
• Before and after trial of 19 HD patients.

• 50mg daily for 4 months.

• The difference in the grade of pruritus before and after sertraline was significant.
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
UV-B Therapy
Uraemic pruritus summary

Moisturisers plus

1. Gabapentin/Pregabalin

2. Evening Primrose Oil

3. UV – B therapy

4. Others.
RESTLESS LEGS SYNDROME
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
Fe

TH

Tyrosine → L-Dopa → Dopamine → DR2
Management

Clonazapem
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)
Pain
Epidemiology of pain in CKD

Dialysis patients – 58 %

Mean weighted prevalence over 36 studies

49 % reported the pain as moderate to severe
Data on PD and conservatively managed patients is more limited but shows similar prevalence and severity figures.
Impact on function and QOL
Impact on QOL

Davison (2002)

69 dialysis patients

62% stated that pain interfered with their ability to participate and enjoy recreational activities.
51% stated that pain caused them “extreme suffering”
41 % stated that pain caused them to consider ceasing Dialysis
Positive correlation with depression

Causes of Pain

ESRD and its treatment

Co-morbidities
1. Pain related to the disease:

- Polycystic Kidney Disease
- Renal Bone Disease
- Amyloid
- Calciphylaxis
2. Pain secondary to treatment:

- PD - recurrent abdominal pain
- AV Fistulae > ‘Steal syndrome’
- Cramps
- Intradialytic headaches
3. Pain related to co-morbidities

- OA
- Diabetic peripheral neuropathy
- PVD / IHD
The patient with pain of multiple causality
Pain etiquette

- ENQUIRE REGULARLY
- RESPOND COMPASSIONATELY
- TREAT COMPETENTLY
- REFER WISELY
Principles of pain management

1. Always enquire about pain.
2. Treat the underlying cause of the pain.
3. Treat the pain meticulously.
4. Treat the pain proportionately.
5. Constantly reassess.
Towards a strategic approach to pain management in patients with CKD
1. There are few studies examining pain management in the specific context of CKD
2. There are international evidence based guidelines and consensus statements on pain management of specific pain syndromes for the whole population.
- Osteoarthritis
- Painful diabetic peripheral neuropathy
- Cancer pain
3. There is an increasing, although not complete, understanding of the pharmacology of analgesic medications in the context of CKD and their dialysability
These recommendations could be filtered through the known pharmacology of medications in the context CKD and their dialysability
Pain syndrome

Evidence based Guidelines and Consensus Statements

Pharmacokinetics/Pharmacodynamics

Pain management for patients in the context of CKD
Davison S, Koncicki H, Brennan F.

Pain in Chronic Kidney Disease: A Scoping Review.

Seminars in Dialysis 2014; 27(2): 188-204.
An approach to pain management in End Stage Renal Disease – Considerations for General Management.

_Seminars in Dialysis_. April 11 2015
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 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.”
7. 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, aged 82 years has ESKD secondary to diabetic nephropathy.

• He 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.”
“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
Case 2

Mr A. G.
A 41 year old man
Type I Diabetes Mellitus diagnosed 2001
Very unstable BSL control
Multiple episodes of DKA
Significant macro and microvascular complications:

Diabetic retinopathy - legally blind
IHD
PVD
Diabetic nephropathy – eGFR 10-15 mls.
Declined dialysis.
Diabetic peripheral neuropathy

Diabetic autonomic neuropathy - Gastroparesis
• Single man. No children.

• Progressive incapacity

• Progressive social isolation

• Admitted to a Nursing Home
Presentation:

1. Significant, intractable nausea and vomiting (up to 20 times per day) over at least 4 months – inadequate response to anti-emetics; PEJ tube inserted.
2. Intractable painful diabetic neuropathy
3. Severe uraemic pruritus
4. Constipation
• Repeated his wish not to commence dialysis.

• Cognitively intact.

• Not depressed.
Initial management

Nausea and vomiting – increased Cyclizine from 50 mg tds to 75 mg tds. Continued Haloperidol. Rotated Domperidone to Maxalon.
For both UP and DPN – Pregabalin 25mg alternate nights.
Approximately one week later presented to A and E in a crisis, highly symptomatic with an eGFR 7.
After discussion with a new Nephrologist at a new hospital patient agreed to commence dialysis as a trial and review regularly.
With the commencement of dialysis there was a:

- Significant improvement of nausea and vomiting – able to remove PEJ tube.
- Onset of Restless Legs syndrome
- Extra-pyramidal signs
- Significant insomnia
Ceased all anti-emetics, cyclizine prn only.
For UP/DPN/RLS –

Gabapentinoid post-dialysis.

For RLS - Clonazepam
Over the next 2-3 weeks significant improvement in all symptoms.
BSLs remained poorly controlled.

- Lantus mane
- Novorapid prior to each meal; range 4-10 units.
The one symptom that intermittently flared, especially nocturnally, was painful DPN
• Gabapentinoid rotation little difference.
• Commenced on low dose Methadone – initially 2.5 mg bd and then increased especially the nocte dose to reflect the diurnal severity of this pain.
• Excellent response
One month after the commencement of dialysis:

"his symptoms have improved dramatically."

Significant sleep dividend.
Remained socially isolated and very lonely
Over the next 3 - 4 months:

- Nocturnal dialysis to increase the dialysis efficiency
- Advance Care Plan made
- On-going symptom management
Family conference

- Even though feeling significantly better than at the commencement of dialysis, QOL remained very poor.

- Decided he wished to withdraw from dialysis. Psychiatry assessment – not depressed.
After attending an important family event, patient ceased dialysis, was admitted to the local Hospice, had a series of farewell meals with his family and died 6 days later.
He requested his insulin continue until he was unconscious. It was then ceased.
Creating and nurturing a Renal Supportive Care service
Annual Renal Palliative Care Symposium

2010 - 2015
Annual Renal Palliative Care Symposium

2016

Sydney, July 29 2016.

Registration : Elizabeth Josland
Elizabeth.Josland@health.nsw.gov.au
Pain Management in patients with End Stage Kidney Disease (ESKD)

Sydney, July 30 2016.

Registration : Elizabeth Josland
Elizabeth.Josland@health.nsw.gov.au
Renal Supportive Care Master Class

2015.
Renal Supportive Master Class

For all clinicians.

Brisbane, August 6 2016.

Registration : Ilse Berquier
Ilse.Berquier@health.qld.gov.au
What are the best materials and books in this area?
Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care

Sara N. Davison¹, Adeera Levin², Alvin H. Moss³, Vivekanand Jha⁴,⁵, Edwina A. Brown⁶, Frank Brennan⁷, Fliss E.M. Murtagh⁸, Saraladevi Naicker⁹, Michael J. Germain¹⁰, Donal J. O’Donoghue¹¹, Rachael L. Morton¹²,¹³ and Gregorio T. Obrador¹⁴
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)
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.
Conclusion

The role of Palliative Care/supportive care in ESRD

A mutual acknowledgement of need.
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
Your patients remain your patients until their death
The family will remember forever your involvement, your demeanour and your compassion