Renal Supportive Care – An Overview

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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 ?


ALBERT NAMATJIRA

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.

DIALYSIS

For patients on dialysis 13.7 % die each year (ANZDATA 2014 Report)

For those aged 75 years and older that figure is 25 %

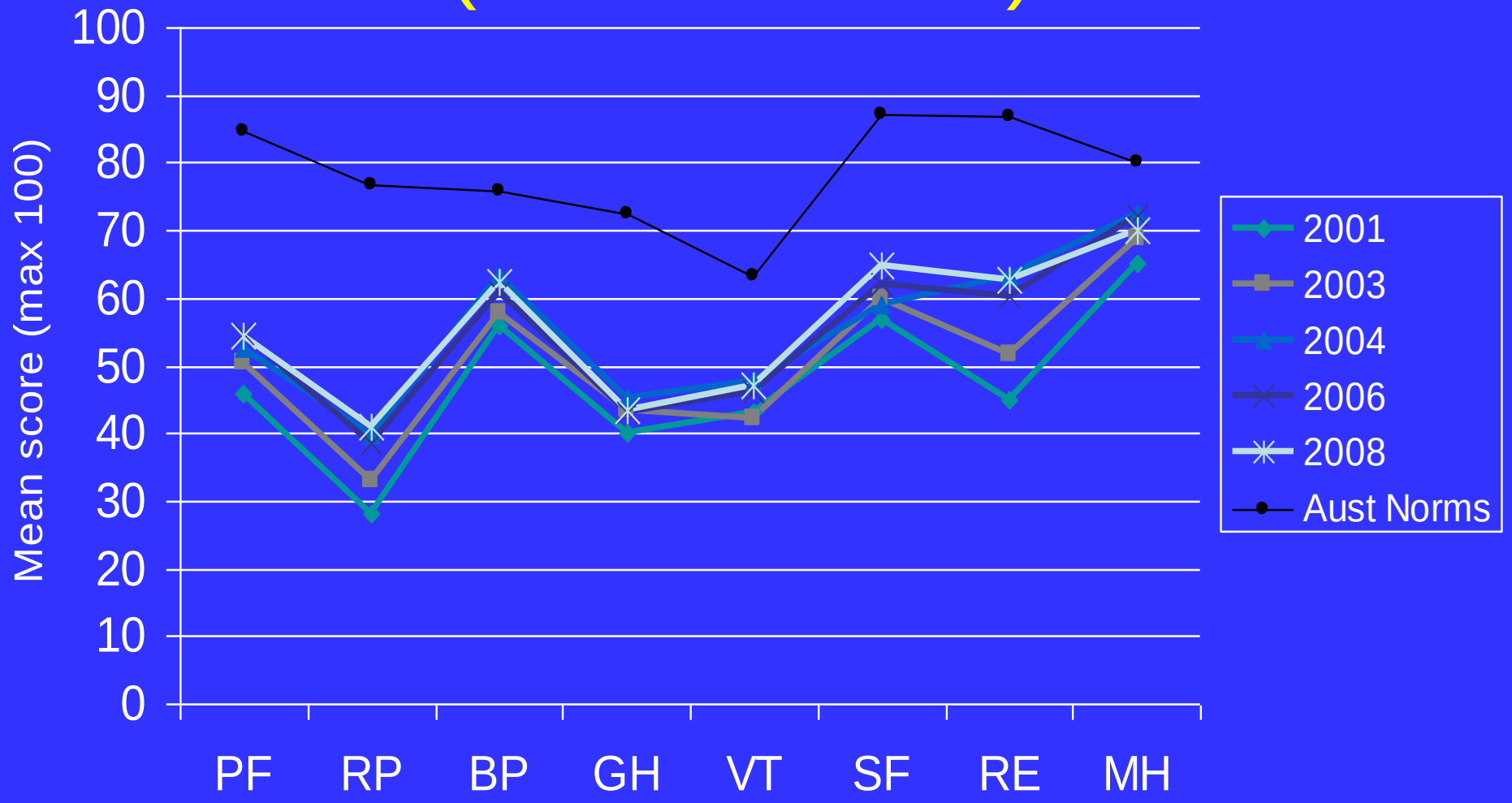
C. Symptomatology

“Patients with CKD, particularly those with ESRD are among the most symptomatic of any chronic disease group.”

Murtagh F, Weisbord S. Symptoms in renal disease. In Chambers EJ et al (eds) *Supportive Care for the Renal Patient* 2010, 2nd ed, OUP.

D. Quality of life

QOL - St George dialysis (SF-36 Scores)



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 examine the various options

RRT

Conservative

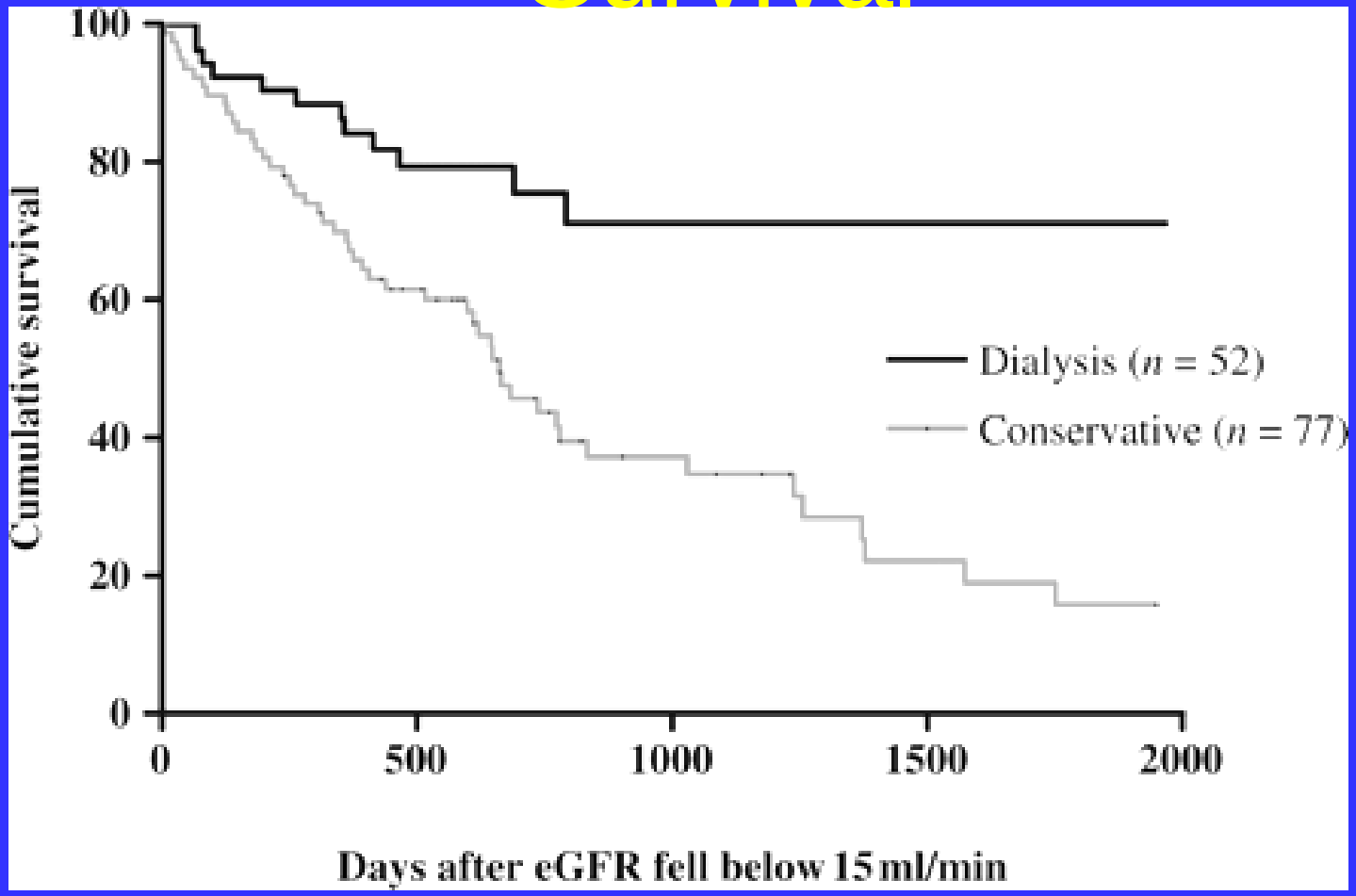
3. Decision making around dialysis

Survival

Dialysis or not ? A comparative study of survival of patients over 75 years with CKD Stage 5.

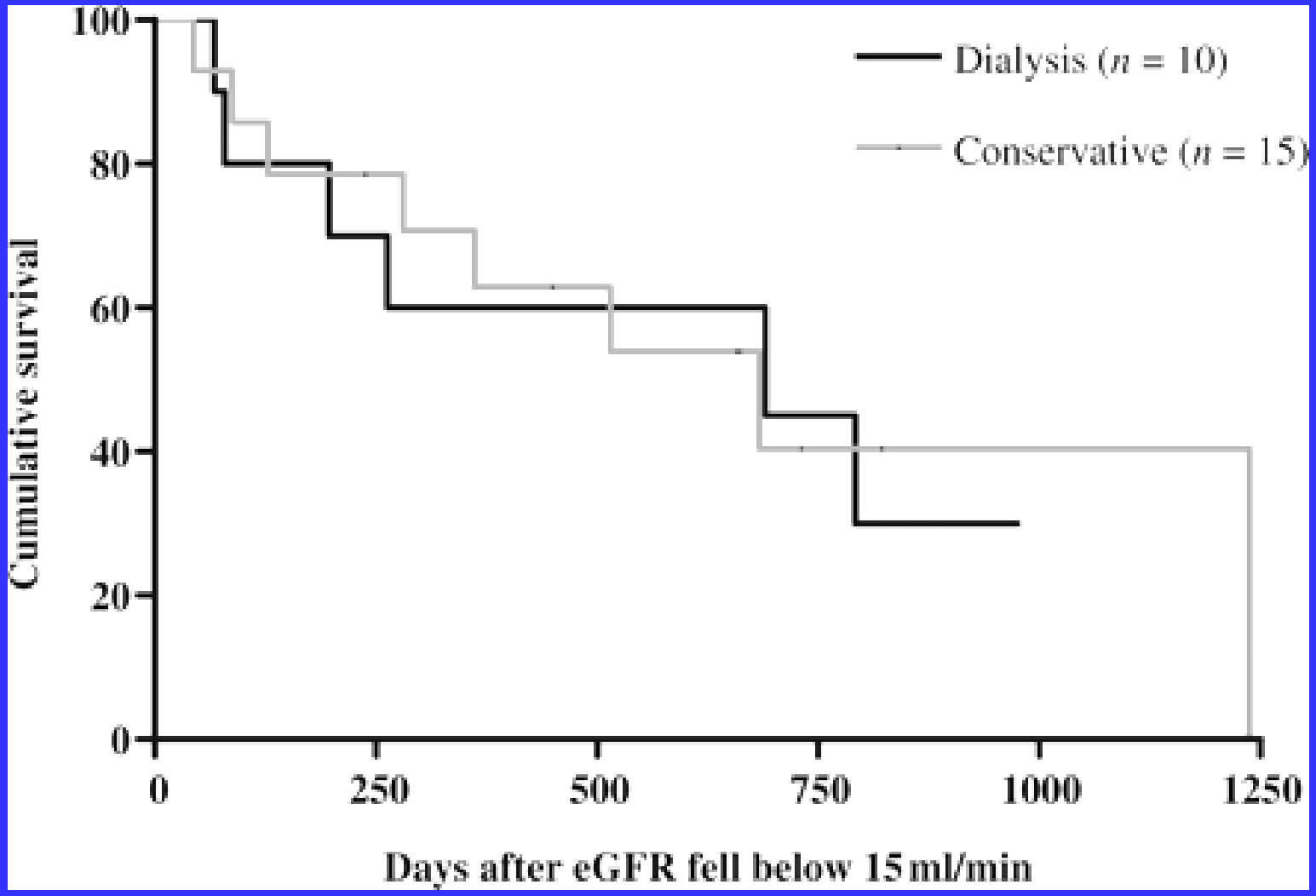
Murtagh FEM et al. *Neprol Dial Transplant* 2007;22:1955-1962

Survival



Murtagh et al. NDT. 2007;22:1955-62

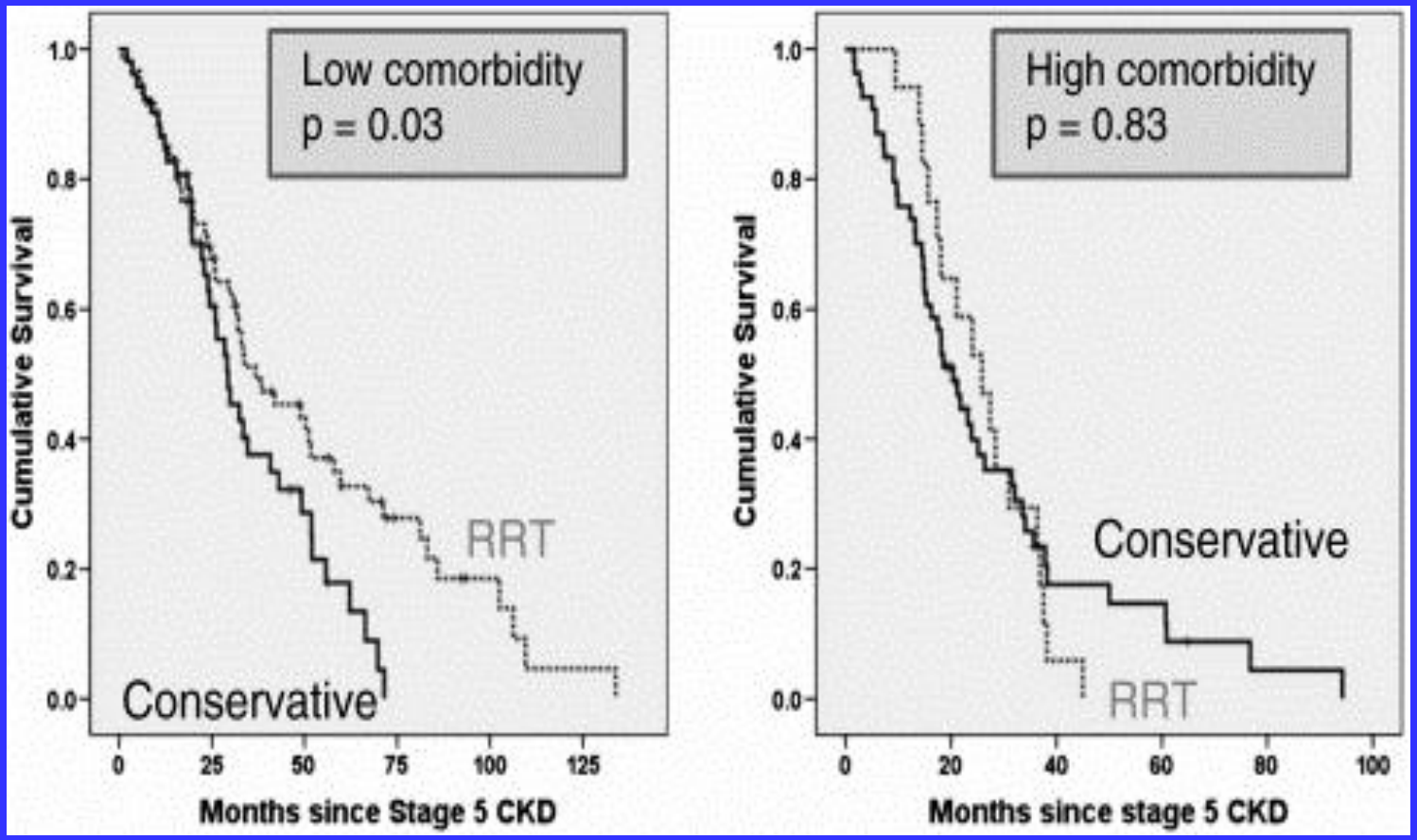
Survival benefit lost if Co-morbidities include IHD



Murtagh et al. NDT. 2007;22:1955-62

RRT v Conservative

Chandra et al NDT Nov 2010



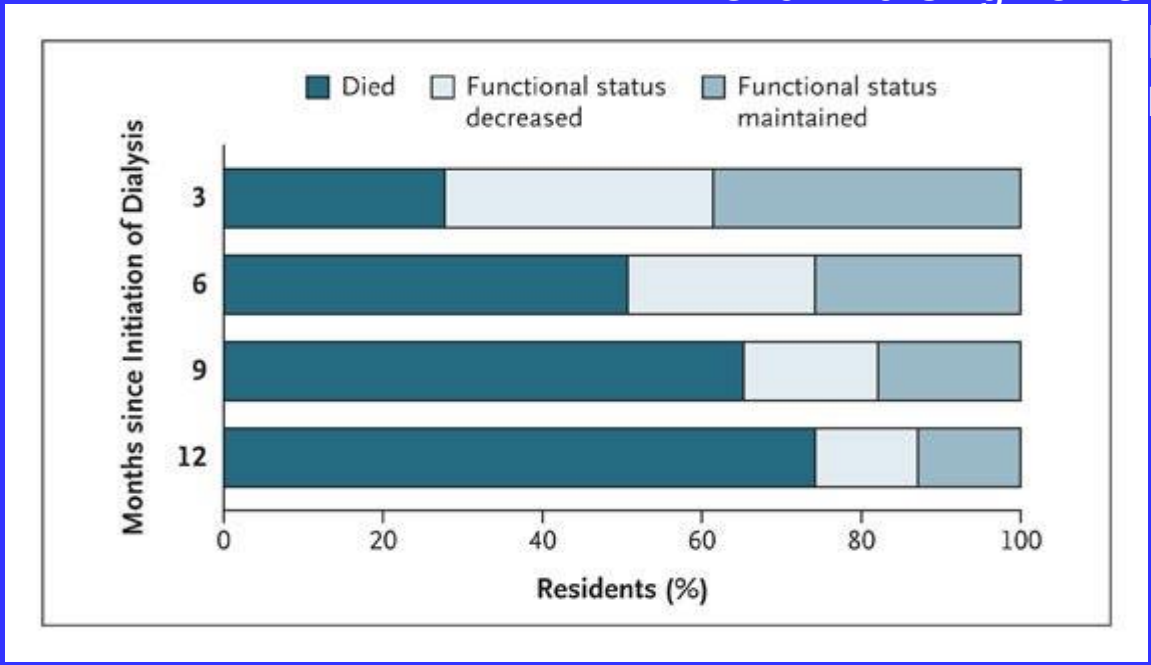
Dialysis in Frail Elders — A Role for Palliative Care

Robert M. Arnold, M.D., and Mark L. Zeidel, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

Volume 361:1597-1598 October 15, 2009

Change in Functional Status after Initiation of Dialysis



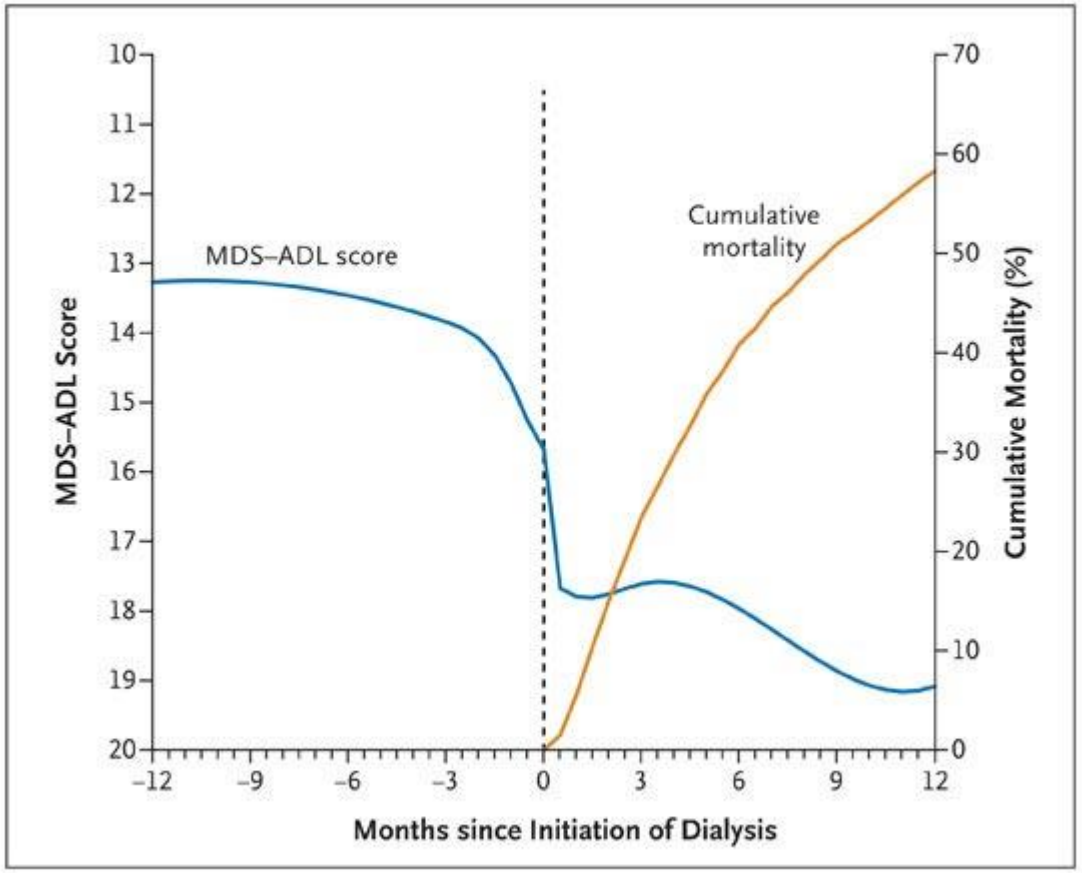
3702 Nursing home residents mean age 73
Mean eGFR 10
Female 60%
Diabetes 68%
CHF 66%
CHD 44%
Cerebrovascular dis. 39%
Depression 35%
Dementia 22%

Kurella Tamura et al. 361 (16): 1539, October 15, 2009

The NEW ENGLAND JOURNAL of MEDICINE

Smoothed Trajectory of Functional Status before and after the Initiation of Dialysis and Cumulative Mortality Rate

[Nursing home residents mean age 73]



Kurella Tamura et al. 361 (16): 1539. October 15, 2009

The NEW ENGLAND JOURNAL of MEDICINE

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**

CJASN 2015; 10 (2) : 260-268

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 (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.)

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

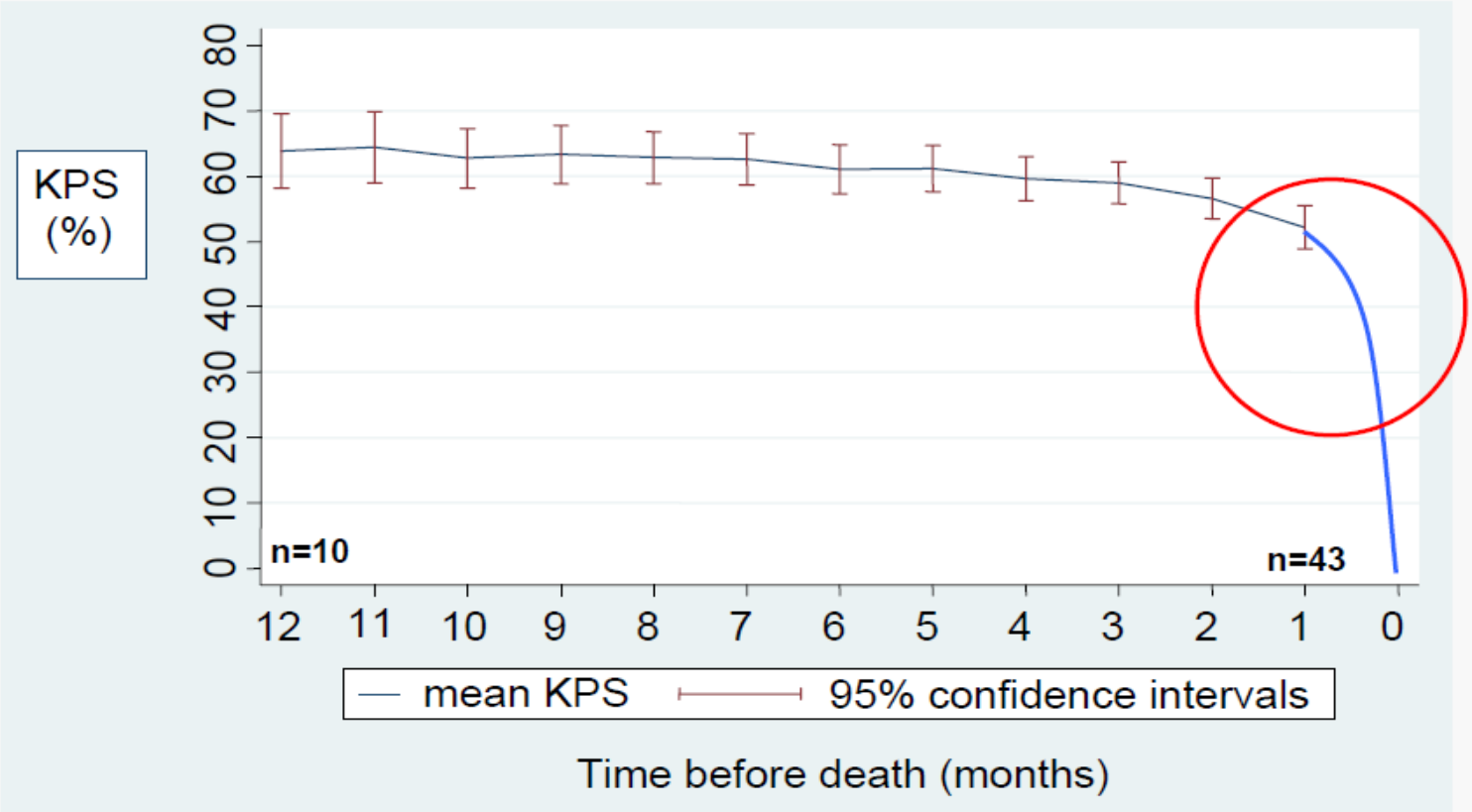
Not simply transfer to Palliative Care

Renal Medicine	Palliative approach
Blood Pressure	
Calcium/Phosphate	Symptom management
Anaemia	Psychosocial support
Fluid balance	Care of the dying

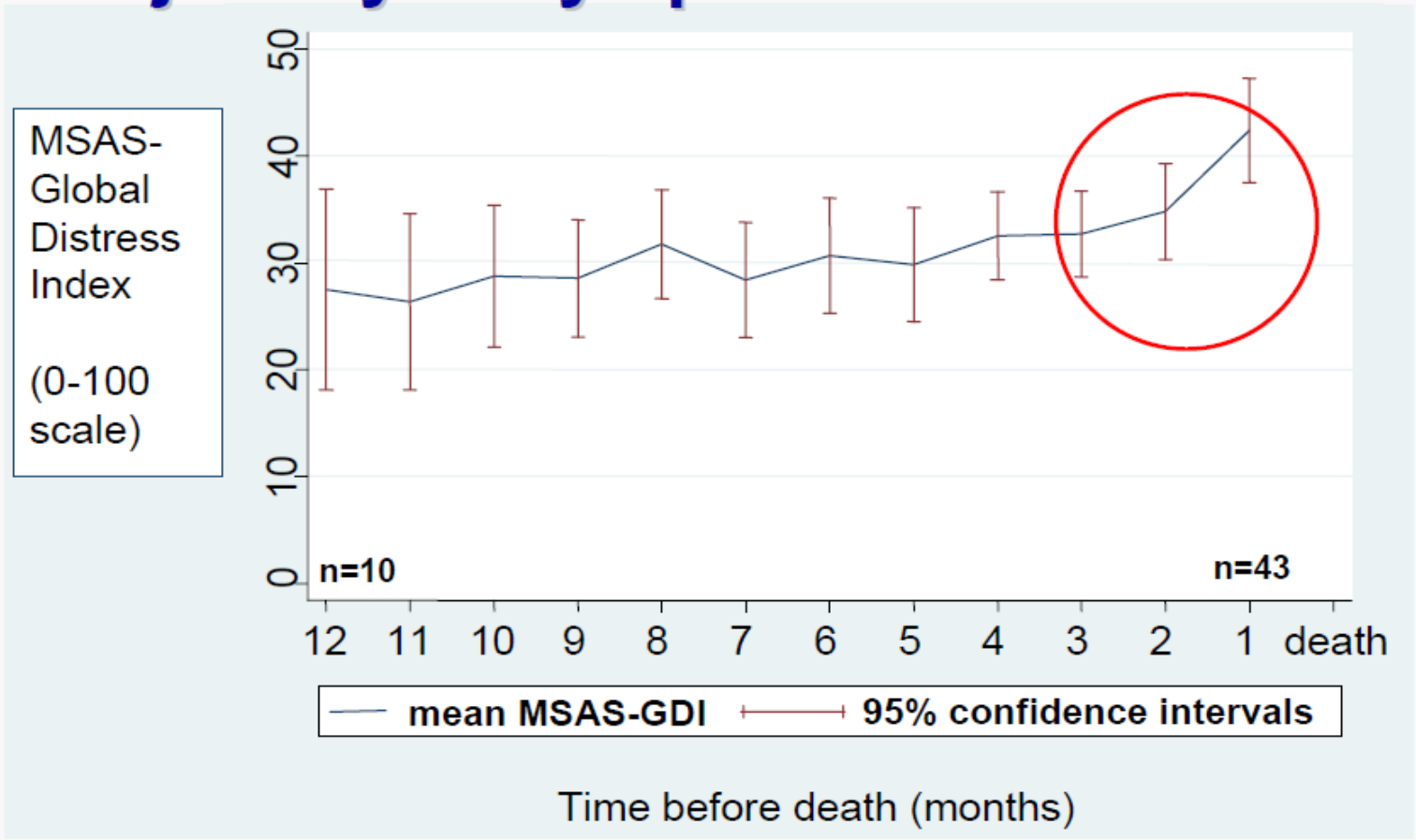
Longitudinal study of conservative stage 5 CKD

- 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)

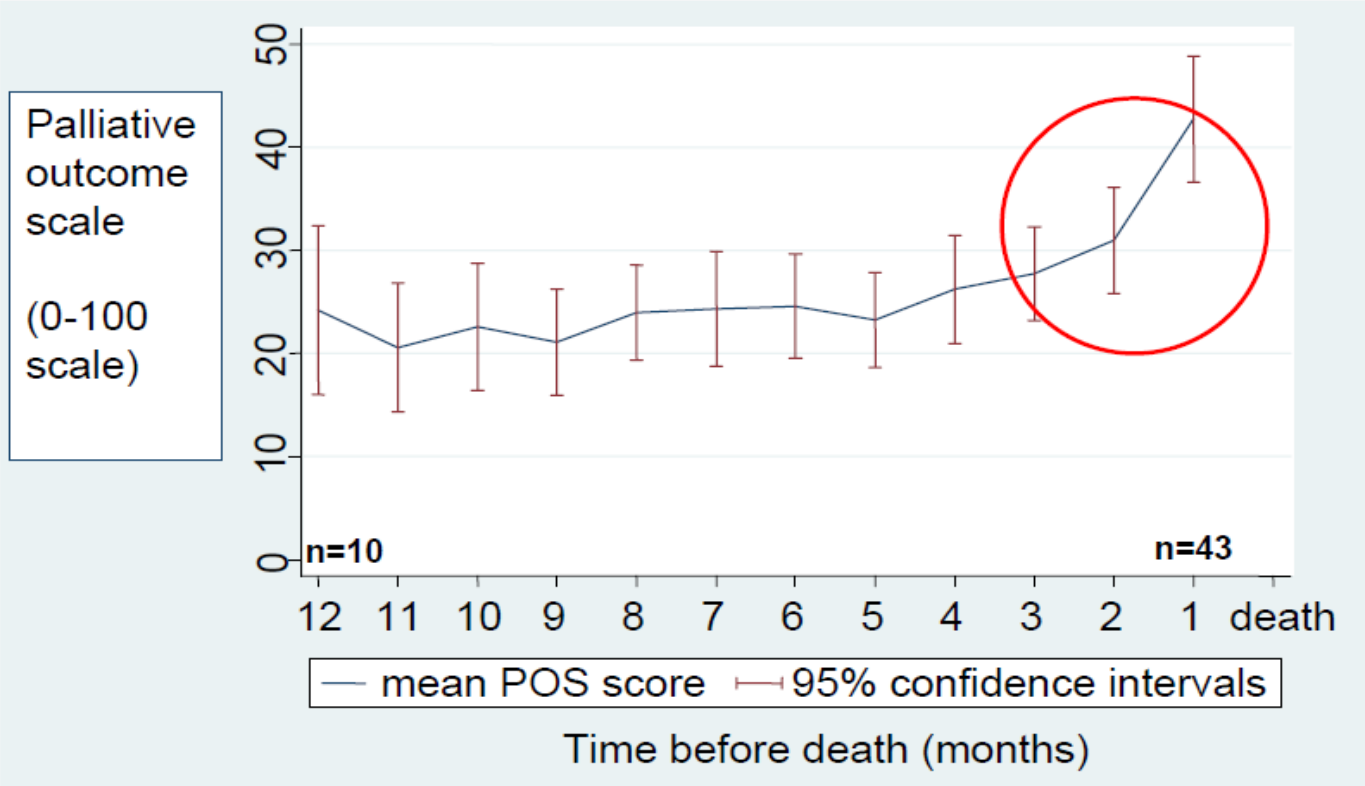
Trajectory of functional status:



Trajectory of symptom distress:



Trajectory of palliative needs:



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

1. Murtagh F et al. A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis *J Pall Med* (2007) 10;6:1266-1276

2. Brennan F et al. The symptoms of patients with CKD stage 5 managed without dialysis. *Progress in Palliative Care* 2015; 23 (5): 267-273.

SYMPTOM PREVALENCE

	Dialysis	Conservative
FATIGUE/TIREDNESS	71%	75%
PRURITUS	55%	74%
CONSTIPATION	53%	
ANOREXIA	49%	47%
PAIN	47%	53%
SLEEP DISTURBANCE	44%	42%
ANXIETY	38 %	
DYSPNEA	35 %	61%
NAUSEA	33 %	
RESTLESS LEGS	30 %	48 %
DEPRESSION	27 %	

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

Pisoni RL, Wikstrom B et al. Neprol Dial Transplant 2006; 21: 3495-3505.

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 → C Fibres → 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.”

Patel TS et al. *Am J Kidney* 2007; 50(1): 11-20.

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

Gabapentin

Gabapentin for uremic pruritus in hemodialysis patients : a qualitative systematic review.

Lau T et al. *Canadian J Kidney Health and Disease* 2016; 3: 14.

“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 doe 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.

Aperis. *J Renal Care* 2010; 36(4): 180-185; Shavit L. *J Pain Symptom Management* 2013; 45(4): 776-781.

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) → PGE2

Arachidonic Acid (AA) → Leukotriene B4

↓

Adrenic Acid

↓

Docosapentaenoic Acid

n- 6 EFA

Linolenic Acid (LA)

↓

Gabba –Linolenic Acid (GLA)

↓

DGLA → PGE1

DGLA → 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.

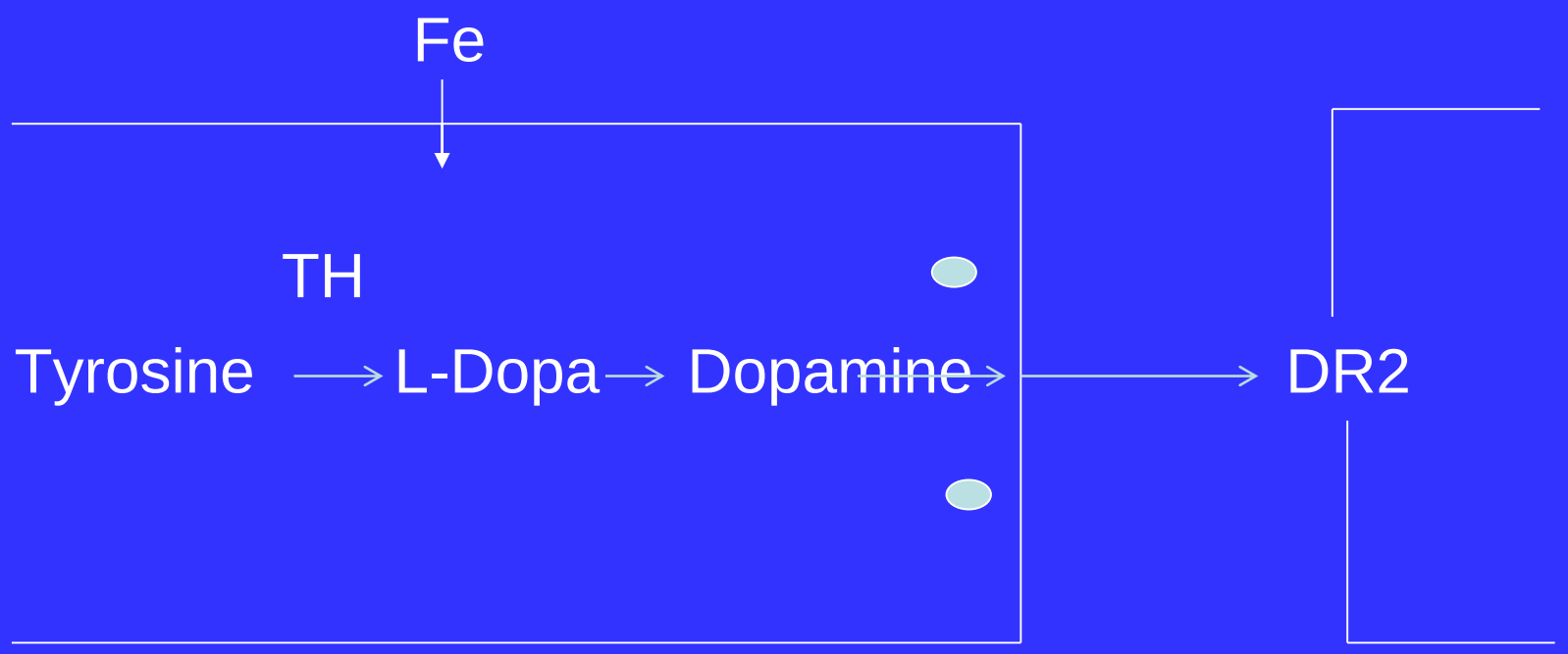
International RLS Study Group – Definition of RLS (1995)

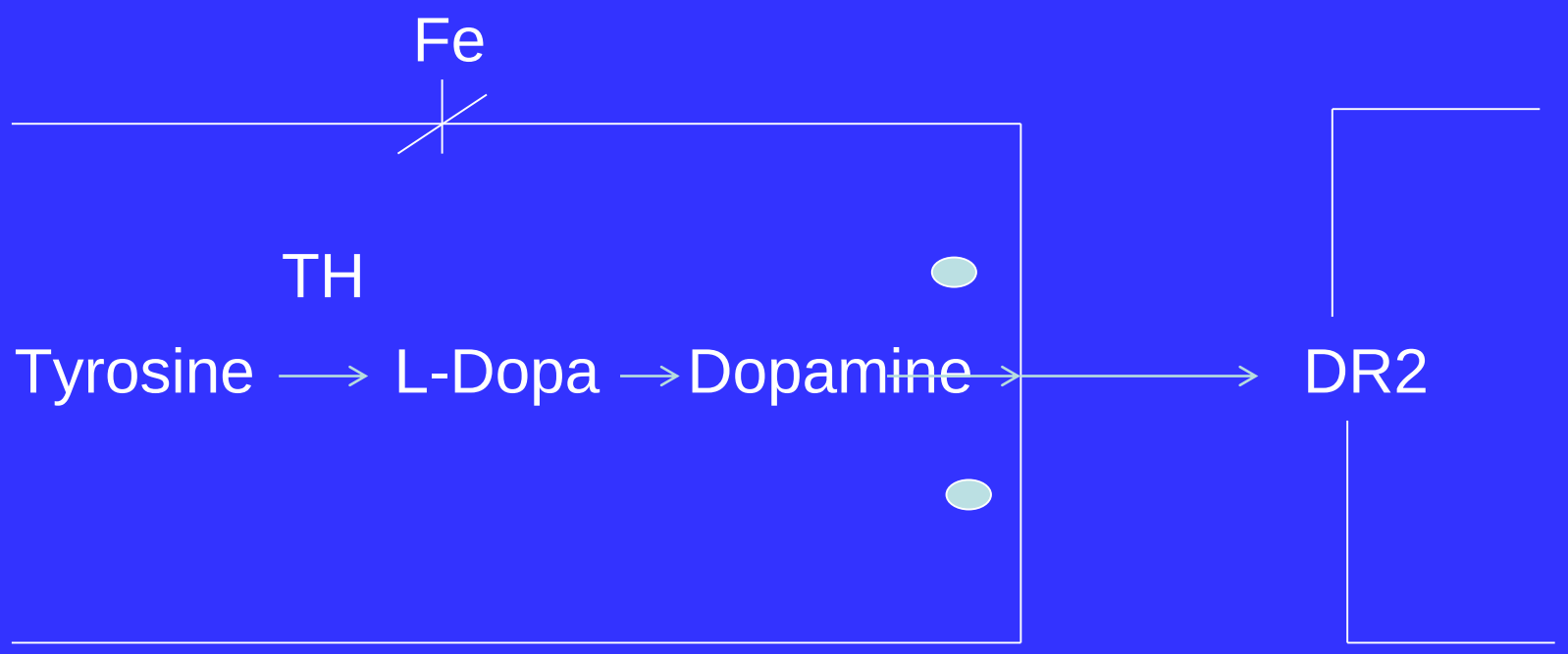
Incidence in the general population :

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 Levo-dopa – Micozkadioglu et al (2004)

Pain

Epidemiology of pain in CKD

Dialysis patients – 58 %

Mean weighted prevalence over 36 studies

Davison S, Koncicki H, Brennan F. Pain in Chronic Kidney Disease : A Scoping Review. *Seminars in Dialysis* 2014; 27(2): 188-204.

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

Davison S, Jhangri GS. J Pain Symptom Management 2005; 30(5): 465-473

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.

Koncicki H, Brennan F, Vinen K, Davison SN.

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.

Nephrologist 1

“Its 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

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 ?

http://www.kidney-international.org meeting report

Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care

Sara N. Davison[1], Adeera Levin[2], Alvin H. Moss[3], Vivekanand Jha[4,5], Edwina A. Brown[6], Frank Brennan[7], Fliss E.M. Murtagh[8], Saraladevi Naicker[9], Michael J. Germain[10], Donal J. O'Donoghue[11], Rachael L. Morton[12,13] and Gregorio T. Obrador[14]

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)

Chambers EJ, Germain M, Brown E (eds)

Supportive Care for the Renal Patient

2nd edition, 2010

Oxford University Press

Brown E, Murtagh F, Murphy E.(eds) *Kidney Disease – From Advanced Disease to Bereavement.* 2nd ed, 2012. Oxford Handbooks.

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