



CKD in Long-term Care

OLTCC Workshop, 2020
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Conflicts of interest

- Received honoraria from Otsuka Canada Pharmaceutical Inc. for Tolvaptan (*Jinarc*) and Patiromer (*Veltassa*) for presentations and drug advisory participation
- These products will not be discussed in today's workshop

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Objectives

• Discuss the significance of low GFR in the LTC resident

- Review common CKD-related **symptoms & management**
- Explore reasons why **dialysis** may or may not be "right" for your patient in LTC

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CKD and usual referral indications

Recommended Reason for Referral:

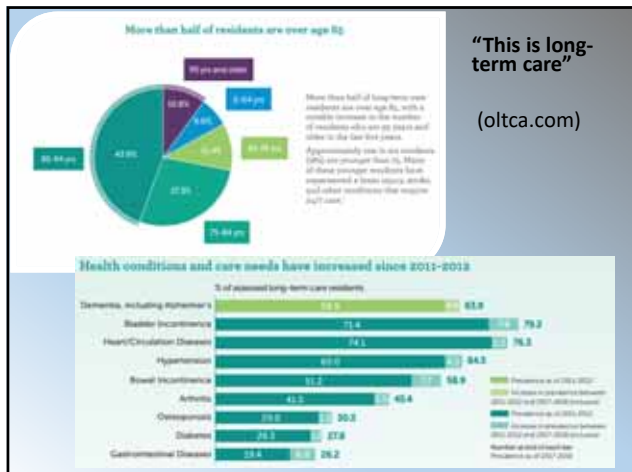
Indications for referral for chronic kidney disease (CKD), including proteinuria:

- eGFR < 30 on 2 occasions, at least 3 months apart, or
- Rapid deterioration in kidney function: eGFR < 45 and decline of > 5 within 6 months in absence of self-limited illness; eGFR must be repeated in 2-4 weeks to confirm persistent decline, or
- Proteinuria: urine ACR > 60 mg/mmol on at least 2 of 3 occasions, or
- 5-year KFR ≥ 3%

GFR categories (ml/min/1.73 m²)
Description and range

Category	Description and range
G1	≥ 90
G2	60-89
G3a	45-59
G3b	30-44
G4	15-29
G5	< 15

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Case #1

80F from LTC

Cr trends
 - May 2017: 131
 - Jan 2018: 129
 - Feb 2018: 197

PMHx

- Left nephrectomy (1980s)
- Alzheimer's dementia
- Crohn's disease (controlled)
- T2DM (25 yrs)
- Gout

MEDS

- Amlodipine 5 mg, Lasix 20 mg daily
- DM: Januvia 25 mg daily, Metformin 500 mg bid, Glucoside 60 mg daily
- Others: Vit B12, Feramax, Tylenol, Rabeprazole

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What is her dialysis risk going forward?
 What should we do about the hyper-K?
 How about the anemia and hyper-PO₄?

Recent course

- Generally weaker over the past months
- Longstanding loose stools, but no acute diarrhea, no blood in the stools
- Oral intake a concern
- No leg swelling
- **Episodes of hyperkalemia**

Labs
 Hgb **78** (MCV 80)
 Cr 197 (eGFR 21), Ur 21; Na 142, K **5.4**, HCO₃ 25, Ca 2.19, **PO₄ 1.7**, PTH 9.1
UACR 50 mg/mmol

Physical Exam
 124/78, HR 62. Overall well-appearing. S1, S2 no murmurs. Breath sounds clear. Abdomen soft, non-tender.

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Case #2

72M progressive renal decline, physical function deterioration -- **pending LTC transfer.**

PMHx

- Extensive PVD with AAA repair / aorto-biiliac bypass
- HTN
- C-spine # 1970s with residual right upper & lower extremity weakness
- COPD (severe)

MEDS

- Amlodipine 10 mg, Bisoprolol 2.5 mg, Atorvastatin, Ventolin, Spiriva, Vitamin D, Ferrous fumarate

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Should this patient be started on dialysis?
What is his future prognosis as a dialysis patient?

<p><u>Recent course</u></p> <ul style="list-style-type: none"> - Progressive weakness - Episodes of nausea affecting appetite - Pruritus - Restless legs 	<p><u>Labs</u></p> <p>Hgb 86 (MCV 95)</p> <p>Cr 548, Na 140, K 4.7, HCO₃ 20, Ca 2.16, PO₄ 1.85, PTH 4.8, Albumin 28</p> <p>(His Cr had rapidly deteriorated over past 6 months from ~250 to 350-400 range).</p>
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Physical Exam

160/77, HR 68. 98% room air. S1, S2 no murmurs. Breath sounds clear. No peripheral edema. JVP 2-3 cm above the sternal angle.


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What is my role as the nephrologist?

- **Diagnose** – Staging CKD and underlying reason
- **Prognosticate** – Estimate trajectory & risk of ESRD
- **Manage** – Intrinsic treatable etiologies & CKD complications

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Diagnosing / Managing / Prognosticating of the aging kidney




- **Diagnosis:** What is chronic kidney “disease”?
- **Prognostication:** challenges in the elderly
- **Management:** philosophic changes relative to goals of care & life expectancy

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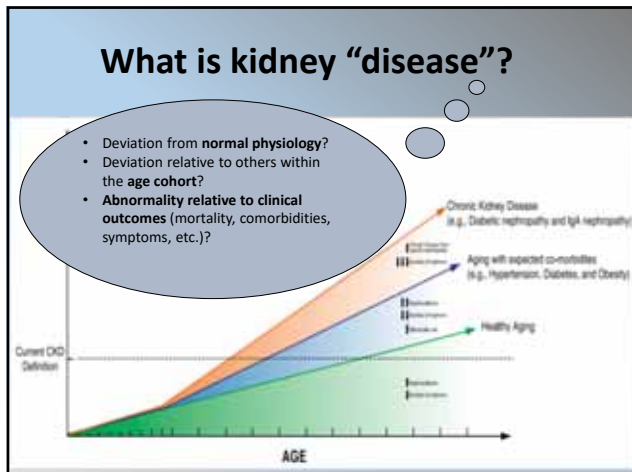
What are we diagnosing?

The kidneys are supposed to decline in function with age....

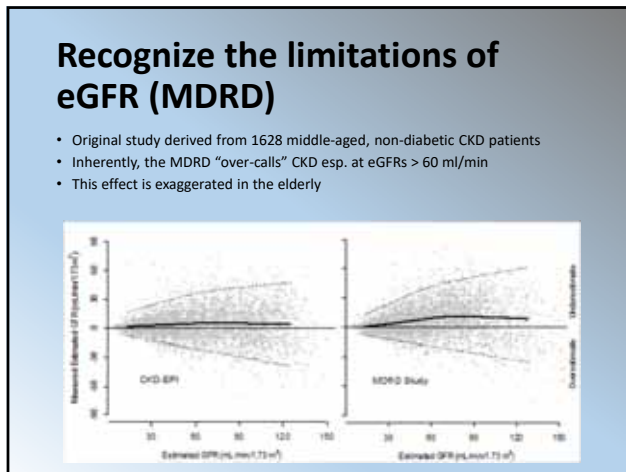
- Renal function declines about **1 ml/min per year** after the **4th** decade of life
- Kidney size decreases by **10% at age 40; by 30% by age 80**



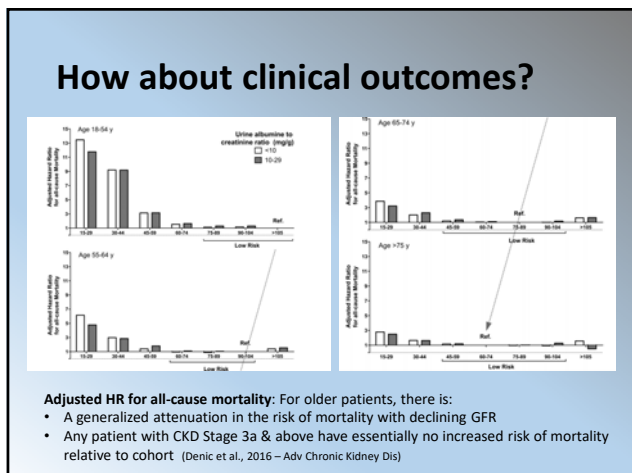
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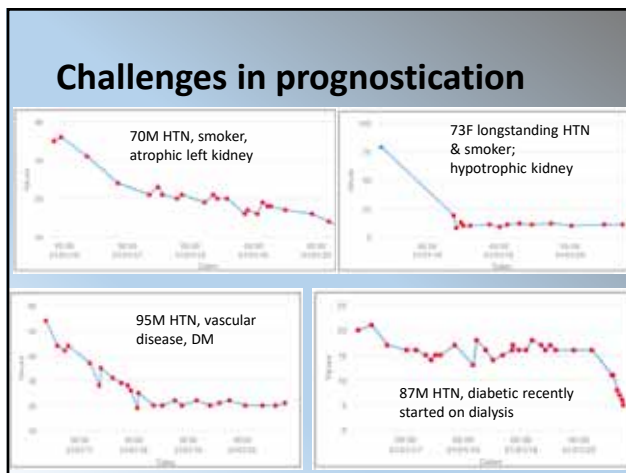
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Kidneys outliving the patient

Age	eGFR	Death /1000 patient yrs.	ESRD / 1000 patient yrs.
75-84	15-29	15.4	6.31
	<15	27.0	44.7
>85	15-29	25.3	2.65
	<15	49.4	29.2

O'Hare et al (2007): 209,622 US veterans' database, patients aged ≥ 75 years with Stage 4 and lower CKD had a higher risk of dying from a competing illness

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- Review common **CKD-related symptoms & management**
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What are we managing?

eGFR (mL/min/1.73 m ²)	N	Hyperparathyroidism	Anemia	Acidosis	Hyperkalemia	Hyperphosphatemia
89-60	74	~10%	~10%	~10%	~10%	~10%
59-50	119	~15%	~15%	~15%	~15%	~15%
49-40	190	~20%	~20%	~20%	~20%	~20%
39-30	252	~25%	~25%	~25%	~25%	~25%
29-20	224	~30%	~30%	~30%	~30%	~30%
<20	185	~35%	~35%	~35%	~35%	~35%

eGFR (mL/min/1.73 m ²)	Description and range	Prevalence
G1	Normal or high	>90
G2	Mildly decreased	60-89
G3a	Mildly to moderately decreased	45-59
G3b	Moderately to severely decreased	30-44
G4	Severely decreased	15-29
G5	Kidney failure	<15

Asymptomatic

Metabolic abnormalities

- Hyper-PTH
- Anemia
- Electrolyte: hyper-K, met acidosis

Uremia*

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CKD complications in context

Complication	Significance?	Rationale / Comments
Anemia	Yes to an extent	Target Hgb 95 – 120 g/L Iron saturation > 20% EPO / oral iron tablets
Electrolytes / acid-base	Yes to an extent	K 6.5 mM = + arrythmia risk Consider discontinuing ACE/ARB/MRA Kayexalate with caution
BMD	Not really	Limited evidence of normalizing values Potential harm with malnutrition
BP / volume	BP – yes to an extent Volume – very important	Individualized approach AHA: sBP < 150 mmHg (HYVET) Volume in relation to comfort / avoidance of pulmonary edema
Uremic symptoms	Very important	Symptomatic management

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Symptoms

Symptom Burden In Patients With ESRD Not Opting For Dialysis

Symptom	% of patients with symptom at baseline (range 7-699 days before death)	1 month prior to death
Lack of energy	76%	86%
Pruritis	74%	84%
Drowsiness	65%	82%
Dyspnea	61%	80%
Pain	53%	73%
Restless legs	48%	65%
Nausea		59%

Murtagh TE, et al. J Pain Symptom Manage 2010

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Uremia

A term to “loosely describe the illness accompanying kidney failure that cannot be explained by derangements in extracellular volume inorganic ion concentrations, or lack of known renal synthetic products”.

Neural and muscular	Endocrine & metabolic	Other
Fatigue	Amenorrhea	Serositis
Peripheral neuropathy	Sexual dysfunction	Itching
Decreased mental acuity	Bone disease	Hiccups
Anorexia	↑ Muscle catabolism	Platelet dysfunction
Altered smell and taste		Relative immunocompromise
Cramps		
Restless legs		
Sleep disturbances		
Coma		
Seizures		

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Uremia ≠ High urea

Table 1. Uremic Solutes.*

Solute Group	Example	Source	Characteristics
Peptides and small proteins	Beta ₂ -microglobulin	Shed from MHC	Not dialyzed because of large size
Guanidines	Guanidinesuccinic acid	Arginine	Increased production in uremia
Phenols	β-Cresol sulfate	Phenylalanine, tyrosine	Protein bound, produced by gut bacteria
Indoles	Indoxyl	Tryptophan	Protein bound, produced by gut bacteria
Aliphatic amines	Dimethylamine	Choline	Large volume of distribution, produced by gut bacteria
Furans	CMRF	Unknown	Tightly protein bound
Peptides	Myristoyl	Dietary intake, cell synthesis from glucose	Normally degraded by the kidney rather than excreted
Nucleosides	Paraoxindole	RNA	Most prominent of several altered RNA species
Dicarboxylic acids	Oxalate	Ascorbic acid	Formation of crystal deposits
Carbonyls	Oxalate	Glycolytic intermediates	Reaction with proteins to form advanced glycation end products

* Uremic solutes may have multiple sources, although only one is listed. MHC denotes major histocompatibility complex, and CMRF 3-carboxy-4-methyl-5-propyl-2-furanproprionic acid.

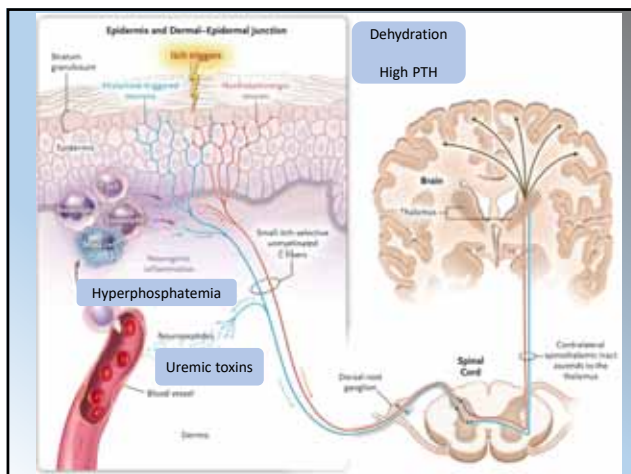
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Pruritus

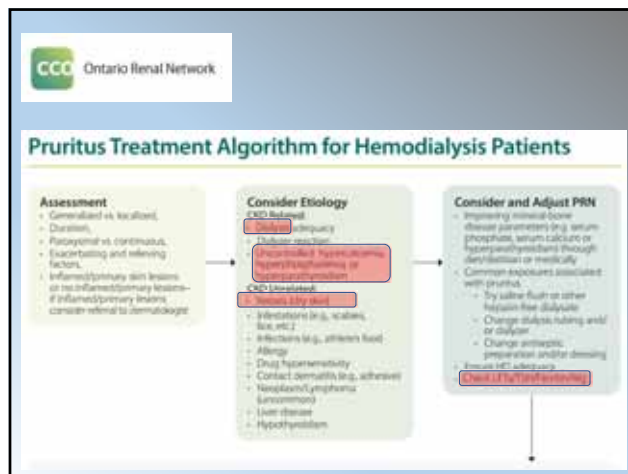
- Affects nearly 50% of patients on dialysis
- Can be experienced in a wide range of ways
- Affects mood, sleep, and social function
- Under-estimated by nephrologists

Factor	Diagnosis		
	No effect	Ameliorating	Exacerbating
Rest	20%	2%	57%
Dry skin	46%	1%	42%
Heat	57%	4%	35%
Sweat	47%	1%	53%
Clustering (eg, wrist)	73%	0%	19%
Soreness	71%	2%	19%
Itching	78%	1%	13%
Before dialysis	73%	0%	13%
Activity	23%	53%	9%
Sleep	46%	46%	0%
Hot shower	33%	44%	4%
Cold shower	32%	39%	2%
Cold	60%	28%	9%
Tiredness	81%	3%	3%
Physical effort	74%	4%	6%
During dialysis	62%	11%	19%
After dialysis	53%	14%	19%

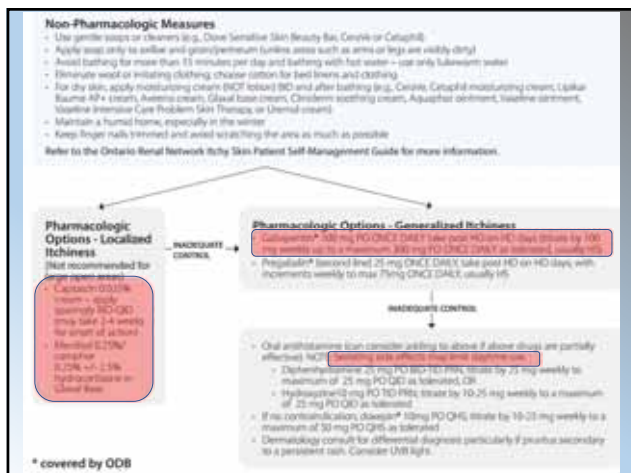
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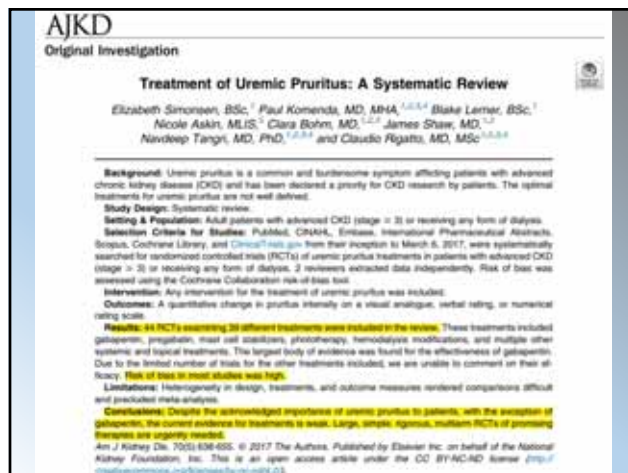
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Restless legs

- Affects 20-40% of dialysis patients and ~25% of CKD patients (Lin et al. 2016)
- Irresistible urge to move the legs
- Relieved by leg movement
- Worse before going to bed
- Associated with poor sleep quality, low quality of life, high risk of CV disease
- Unclear mechanism (?dopaminergic system dysfunction)

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Assessment
Timing: especially at night or during dialysis, alleviating and exacerbating factors (e.g., pain, pulling, itching, need to move, pins and needles, cramping, etc.), and effect on sleep or other symptoms (e.g., anxiety and depression)

Non-Pharmacologic Measures
 • Discontinue or reduce standing time, if feasible
 • Correct iron deficiency – may prevent initial augmentation with dopaminergic therapy
 • Encourage good sleep hygiene
 • Stretching, massage, or exercise (including anaerobic exercise)
 • Hot/cold water or towel
 • Distracting attention (e.g., with puzzle)
 • Limit caffeine/alcohol
 • Smoking cessation
 Refer to the Ontario Renal Network Restless Legs Syndrome Patient Self-Management Guide for more information.

Consider Etiology
 • Anemia (including iron deficiency, hemolytic, chronic kidney disease)
 • Depression and Anxiety
 • Medications (antidepressants, antipsychotics, antiemetics, anti-nausea, parenteral iron)
 • Antidopaminergics (anticholinergics up to 25% or 50% or 75% of the dose, clonidine, metoprolol, fluoxetine, paroxetine, sertraline, duloxetine, venlafaxine)
 • Stimulants, alcohol, caffeine, nicotine
 • Others: TCA, carbamazepine, lithium
 Assess individual contributing factors
 • Sleep deprivation
 • Positive family history
 • Rheumatoid arthritis or Sjogren's
 • Pregnancy

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Pharmacologic Options
(If RLS symptoms occur during HD, give medication prior to HD)

AVOID opioids and quinolones

- **For intermittent RLS:** **pramipexole** 100/200 mg tablet – 1x tablet PO HD, titrate Q3-7 days to effect up to 200/100 mg PO HD. If patient awakens in middle of the night with RLS, use CR formulation (levodopa doses <300 mg may increase risk of augmentation – see dopamine agonists below for definition).
- **For daily RLS:** dopamine agonists
 - Compared to levodopa, has decreased risk of augmentation (i.e., paradoxical increase in RLS symptoms caused by medication) but increased incidence of agitation and nausea. If augmentation occurs, consider reducing dose, splitting dose or trying rotigotine. Caution with rotigotine as multiple dosing is not recommended.
 - **pramipexole** 1.25 mg PO 2 hours prior to HD, increase by 0.25 mg PO Q7 days to effect up to a maximum of 4 mg/day
 - **ropinirole** 1.25 mg PO 2 hours prior to HD, may increase by 0.125 mg PO Q7 days to effect up to a maximum of 1.75 mg/day
- If ineffective with dopaminergic agent or RLS with painful neuropathy:
 - **gabapentin** 300 mg PO Q7 days to a maximum of 300 mg PO HD
 - **pregabalin** 25 mg PO Q7 days to a maximum of 75 mg PO HD

INADEQUATE CONTROL

- **Benzodiazepines**
 - Preferably avoid secondary to potential for dependency, questionable efficacy and adverse effects (due to clonazepam's long half-life). If severe insomnia, refer to Insomnia Treatment Algorithm. Use with caution in the elderly.
 - **Clonazepam** 0.5 mg PO HD, titrate by 0.1 mg Q7 days to a maximum of 2 mg PO HD
- **Clonidine** 0.05 mg PO HD if patient is not hypertensive or bradycardic

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www.ontariorenalnetwork.ca

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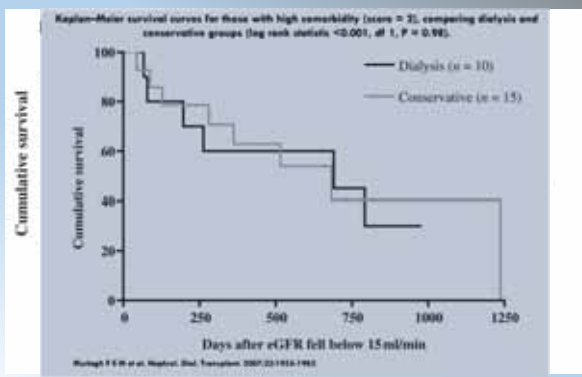
Will dialysis extend life?

- O'Connor & Kumar (2012) – Systematic review, Median survival of **6.3 – 23.5 months**
- Shortest survival in patients with already extensive comorbidities and functional decline
 - Longer survival in younger patients
 - **Stoke comorbidity score** – malignancy, ischemic heart disease, PVD, LV dysfunction, DM, collagen vascular disease, other significant pathology (**score of 2 = 56% survival at 1 year**; HR 2.5 for each incremental increase)

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Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5

Filo E. M. Murtzagh¹, James E. Marsil², Paul Donohoe³, Nairul J. Ekbal⁴, Neil S. Sheerin⁴ and Fiona E. Harris²



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Predicting Six-Month Mortality for Patients Who Are on Maintenance Hemodialysis

Calculate
Version 4.1

3-Month Mortality in Incident Elderly ESRD Patients

Estimate the risk of early death (at 3 months) in elderly patients starting dialysis.

Search for conditions: [Elderly Incident ESRD] [Predicting 3-Month Mortality for Incident Elderly ESRD Patients]

Selected conditions: [Elderly Incident ESRD] [Predicting 3-Month Mortality for Incident Elderly ESRD Patients]

Age: [75-84]

Gender: [Male]

Estimated Mean Survival: [0.50]

Calculate

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Dialysis as a "palliative" treatment

Dialysis is a palliative treatment

- Offers symptom relief
- That sustains quality of life until the patient is ready to die
- That offers relief from symptoms such as those arising from uremia, itching, drowsy, SOB, Nausea, legs, etc.

Symptom Burden In Patients On Dialysis

% of patients on dialysis experiencing moderate to severe symptoms. n = 507

Symptom	% of patients on dialysis experiencing different symptoms
Tired	74%
Poor well-being	60%
Poor appetite	49%
Pain	48%
Itching	46%
Drowsy	45%
SOB	34%
Nausea	25%

Shotton S, et al. *Kidney International* 2008.

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Changes in Quality of Life during Hemodialysis and Peritoneal Dialysis Treatment (Quality and Disease Specific Measures)

Table 4. Change in overall health status* from baseline to 1 year after baseline in 724 CHOICE patients overall and stratified by modality

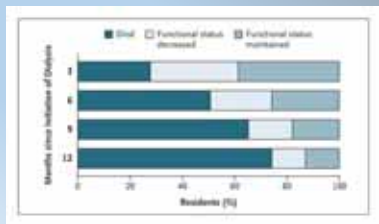
Domain	Overall			HD			PD			p†
	%	% No. Improved	% No. Improved	%	% No. Improved	% No. Improved	%	% No. Improved	% No. Improved	
General (SF-36)	27	32	21	27	31	22	29	34	18	0.6
physical function	22	26	21	23	28	21	25	29	21	0.8
bodily pain	28	46	26	28	46	25	26	47	27	0.8
general health	23	48	19	23	50	20	21	43	16	0.5
vitality	27	49	24	27	49	24	29	46	25	0.7
social function	28	38	21	30	39	21	22	37	21	0.9
role emotional	38	42	28	39	41	28	36	43	27	0.9
mental health	23	37	20	24	37	19	21	37	22	0.5
PCS	31	42	27	31	42	27	32	43	25	0.9
ACS	26	48	26	27	48	25	24	49	27	0.7
USRD										
symptoms	23	37	19	23	36	19	23	39	18	0.7
cognitive function	26	36	17	27	36	17	25	36	19	0.8
sleep	24	37	19	23	37	20	27	36	17	0.5
sex	30	30	20	30	30	20	30	30	20	0.9
body image	19	43	16	19	44	17	18	49	13	0.5
quality of life	24	37	19	24	37	19	23	38	17	0.5
frailty	22	39	19	22	39	19	20	39	21	0.6
travel	25	38	17	25	38	17	21	40	17	0.5
occupation	22	41	17	22	40	18	21	43	14	0.4
exercise	23	41	18	23	41	17	18	43	19	0.3
work	23	38	19	24	38	18	19	35	23	0.1
diet	24	40	17	25	38	17	21	42	17	0.5
house	28	44	19	21	43	16	16	47	17	0.3
access	22	34	24	23	33	24	19	38	23	0.4

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Dialysis in the LTC population

Functional Status of Elderly Adults before and after Initiation of Dialysis

Shotton S, et al. *Kidney International* 2008.



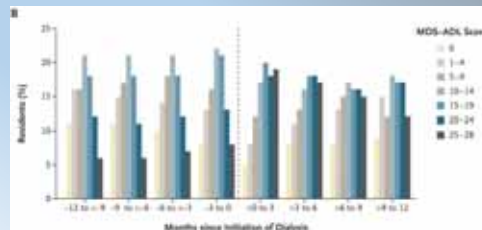
3702 NH residents in US over 2-year period.

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3702 NH residents in US over 2-year period.

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Palliative dialysis

	Conventional dialysis	Palliative dialysis	Conservative management
Uremic control	Minimize functional uremic toxins (UUR or Kt/V)	CrCl can vary by percent of preserved kidney; symptom and response need be for symptoms, at risk of complications	NA
Bleed removal / dialysis adequacy	Optimize treatment duration and frequency designed to achieve adequacy targets	Palliative dialysis treatment scheduled to minimize symptoms of uremia and treatment burden, not to achieve specific adequacy targets	NA
Fluid management	Limit fluid intake to minimize interdialytic weight gain; diuretic treatment and prescribed to achieve specific target weight; diuretic may be used to maintain urine output	Limited fluid intake as necessary to reduce symptoms of fluid overload; diuretic treatment to minimize symptoms and maintain function; use to achieve specific target weight; diuretic may be used to maintain urine output	Limited fluid intake as necessary to reduce symptoms of fluid overload; diuretic may be used to maintain urine output
Dietary restrictions	Dietary counseling, avoidance of potassium, sodium, and phosphate; ensure adequate protein intake	Dietary restriction only to the extent that they help relieve symptoms and improve quality of life	NA
Mineral and bone disorder management	Use of phosphate binders, vitamin D analogs, and calcimimetics as necessary to achieve targets for PTH, calcium, and TSH levels	Limited use of medications, use driven by need to address SMD parameter targets	NA
Anemia management	Administer to iron and EPO to prevent need for transfusions and achieve targets for Hb and TSH levels	Administration of iron and EPO only as needed to prevent need for transfusions and minimize symptoms of anemia that impact quality of life	NA
Cardiovascular disease management	Treat hypertension and dyslipidemia	Limited use of medications to treat hypertension or dyslipidemia	NA
Pain management	Management of pain as needed	Management of pain as priority	NA

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What is her dialysis risk going forward?
What should we do about the hyper-K?
How about the anemia and hyper-PO₄?

1) Repeat Cr/Ur; UACR - ?pre-renal

- Return comes back 150 (eGFR 30); UACR 50
- KFRE: 5% 2 years, 15% 5 years
- Overall lifetime risk of HD is LOW
- **Hyper-K:** watch for dehydration; dietary restriction
- **Anemia:** check iron, replace to iron sat 20%. Consider ESA.
- **High PO₄ / PTH:** Generally don't worry about it unless symptomatic w pruritus

Labs
Hgb **78** (MCV 80)

Cr 197 (eGFR 21), Ur 21; Na 142, **K 5.4**, HCO₃ 25, Ca 2.19, **PO₄ 1.7**, PTH 9.1

UACR 50 mg/mmol

Cr trends

- May 2017: 131
- Jan 2018: 129
- Feb 2018: 197

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Should this patient be started on dialysis?
What is his future prognosis as a dialysis patient?

Cohen score: ~50% survival on hemodialysis at 6 months

HD did improve his symptoms initially but continued to have ongoing pruritus, fatigue

Admission Aug 2018 – COPD exacerbation

Ongoing decline Aug – Dec 2019. Regular goals of care discussions.

Finally, Dec 15, 2019 – pneumo-sepsis, patient withdrew care

Labs
Hgb **86** (MCV 95)

Cr 548, Na 140, K 4.7, HCO₃ 20, **Ca 2.16**, **PO₄ 1.85**, PTH 4.8, Albumin 28

(His Cr had rapidly deteriorated over past 6 months from ~250 to 350-400 range).

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Summary

Significance of low GFR	Symptoms & management	Why (if?) dialysis
<ul style="list-style-type: none"> Think of Kidney "Disease" in relation to meaningful outcomes relative to patient... NOT an eGFR Majority of patients in LTC will die from competing causes rather than go on to ESRD 		

Graph showing threshold eGFR vs age group. The threshold eGFR decreases from ~50 at age 18-44 to ~10 at age 85-100. The area above the threshold is shaded black and labeled 'Risk of death-risk of ESRD'. The area below the threshold is shaded grey and labeled 'Risk of ESRD-risk of death'.

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Summary

Significance of low GFR

- Think of Kidney "Disease" in relation to meaningful outcomes relative to patient... NOT an eGFR
- Majority of patients in LTC will die from competing causes rather than go on to ESRD

Symptom	% of patients with symptoms	% of patients in dialysis
Lack of energy	79%	86%
Pruritus	64%	84%
Dyspnea	61%	87%
Pain	63%	89%
Restless legs	60%	81%
Itching	60%	84%

Why (if?) dialysis

- Think of lab work in relation to symptoms
 - Hgb > 95 (EPO, iron)
 - K < 5.5 mM
 - Volume control is very important
 - "Sensible targets" for BP, Ca / PO₄
- Attention to "uremic" symptoms: pruritus, restless legs – algorithm for ORN

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Summary

Significance of low GFR

- Think of Kidney "Disease" if meaningful relative to patient... NOT an eGFR
- Majority of patients in LTC will die from competing causes rather than go on to ESRD

Why (if?) dialysis

- Dialysis in the LTC population offers **limited increase quantity** of life
- No assurance it will improve **quality**
- In select cases, an **individualized dialysis regimen** may be reasonable

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QUESTIONS?

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