

HHP Care Model and Disease Management Webinar Series

Chronic Kidney Disease (CKD) #4

Thursday, December 2, 2021

5:30pm – 6:30pm

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Moderator – 12/02/21

Andy Lee, MD

Medical Director, *Hawai'i Health Partners*

Chief of Staff, *Pali Momi Medical Center*

Hawai'i Pacific Health

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 - Due to time constraints, any unanswered questions will be addressed this week and posted on the HHP website
- A recording of the meeting will be available tomorrow on the HHP website and intranet.

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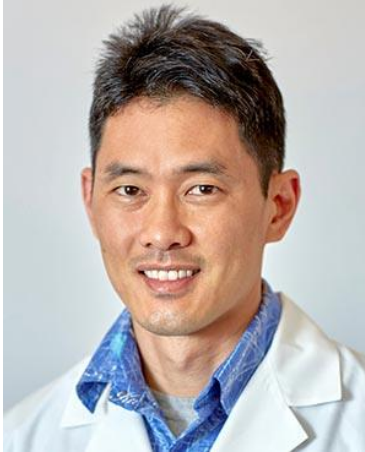


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Renal Replacement Therapy Options/Management, What a PCP Should Know



Rick Hayashi, MD

Nephrologist, Hawai'i Kidney Specialists
Assistant Clinical Professor of Medicine
– John A. Burns School of Medicine,
University of Hawaii



Marti Taba, MD

Primary Care Physician – Family Medicine,
Straub Kailua Family Health Center
Hawai'i Pacific Health Medical Group

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Introduction to Chronic Kidney Disease (CKD)

- Epidemiology of CKD
- Identifying CKD
- Accurately assess kidney function and estimate risk for progression
- Determine cause of CKD
- Take measures to slow down progression of CKD
- Identify and treat secondary complications of CKD
- **Renal replacement therapy options/management**

Summary of last presentation – Secondary complications of CKD

- Bone disease in CKD is more than just about bone protection, in particular increased CV risk. Identify low versus high bone turnover state. Prevent metabolic complications from progressing early on, before they become severe.
- Treat anemia of CKD cautiously due to increased stroke and malignancy risk. Target hgb 10-11. HIF-PHI inhibitor are an oral ESA but are not better or safer than traditional EPO.
- CKD is a CV risk equivalent
- IV iron therapy with HF and CKD shows improved HF outcomes.
- New K binders are safer than SPS and can allow continuation of evidence based medications like ACE-I/ARBs and spironolactone
- Symptoms of uremia can start to occur when the eGFR is <15mL/min

Race and eGFR

- >90% of labs use a race modifier that inflates the eGFR in Blacks versus non-Blacks.
- The Black race coefficient was derived from differences noted in endogenous measurement of creatinine or from exogenous iothalamate clearance.
- Use of race can contribute to systemic racism in medicine.
 - Inequitably inflates GFR estimates in Blacks
 - Lacks a biological basis.

Race and eGFR

- Inker et al.
 - Compared new eGFR(Cr alone and Cr + cystatin C) equations that eliminated race and compared them with 2009 CKD-EPI and 2012 CKD-EPI + cystatin C equations versus measured GFR.



Race and eGFR

- Inker et al.- Results
 - 2009 CKD Epi eGFR Cr equation (includes race) overestimated eGFR in Black participants by median of 3.7mL/min but had negligible bias in non-black participants
 - When race factor omitted, the equation underestimated eGFR in Blacks by 7.1mL/min
 - New equation using Cr (but no race) underestimated eGFR in blacks by 3.6mL/min and overestimated eGFR in non-blacks by 3.9mL/min
 - New CKD EPI Cr + cystatin C eGFR (without race) equation had less bias and higher agreement



Race and eGFR- Findings

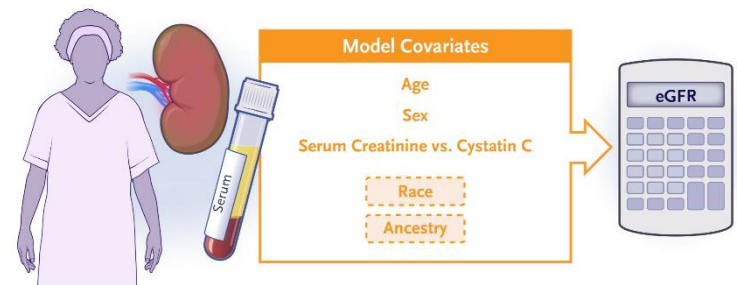
- Hsu et al.
 - Used CRIC database with reported race, genetic genotyping, cystatin C and Cr values compared with iothalamate measurement of GFR as a reference

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ORIGINAL ARTICLE

Race, Genetic Ancestry, and Estimating Kidney Function in CKD

C. Hsu, W. Yang, R.V. Parikh, A.H. Anderson, T.K. Chen, D.L. Cohen, J. He, M.J. Mohanty, J.P. Lash, K.T. Mills, A.N. Muir, A. Parsa, M.R. Saunders, T. Shafi, R.R. Townsend, S.S. Waikar, J. Wang, M. Wolf, T.C. Tan, H.I. Feldman, and A.S. Go, for the CRIC Study Investigators*

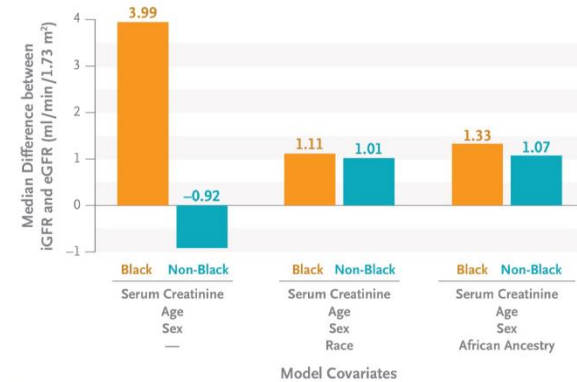


Model Performance and Race Coefficients from GFR Estimating Equations Based on Serum Creatinine

Race and eGFR- Findings

- Hsu et al.
 - Using Cr alone and leaving out race, underestimated eGFR in black participants but did not affect non-black participants
 - When cystatin C was used, eGFR estimates were similar in black and non-black participants. Race did not impact accuracy

Model Performance and Race Coefficients from GFR Estimating Equations Based on Serum Creatinine



Model Performance and Race Coefficients from GFR Estimating Equations Based on Serum Cystatin C



CONCLUSIONS

Cystatin C–based equations rather than creatinine-based equations allowed for sufficiently accurate GFR estimates in Black and non-Black participants without the need to incorporate race.

Race and eGFR – conclusions

- New Cr based eGFR equation without race underestimate eGFR in blacks and overestimates eGFR in non-blacks
- Cystatin C is required to more accurately measure eGFR without race factor.
- Use 2021 CKD-EPI Cr Cystatin C calculator (does not include race) to determine eGFR
- https://www.kidney.org/professionals/kdoqi/gfr_calculator

Race and eGFR – Conclusions

- The eGFR cannot be used in isolation but must be interpreted in the context of a holistic view of the patient's entire clinical situation.
- Factors to consider...
 - eGFR trend
 - Albuminuria/urinary sediment
 - Abnormalities in body/muscle mass
 - Volume status
 - Underlying medical conditions

Renal Replacement Therapy Overview

- Kidney transplant
- Dialytic therapies
 - Peritoneal dialysis
 - Home hemodialysis
 - In-center hemodialysis
- Dialysis in the elderly/supportive care

Kidney Transplant

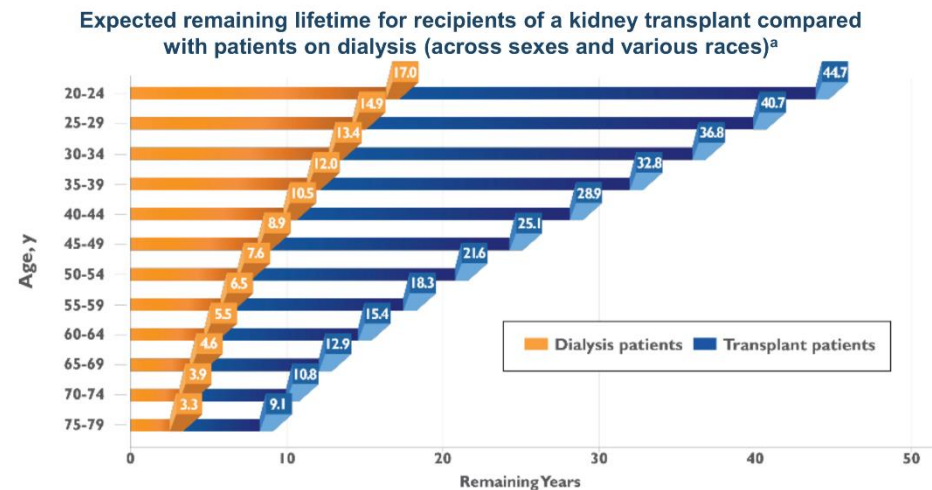
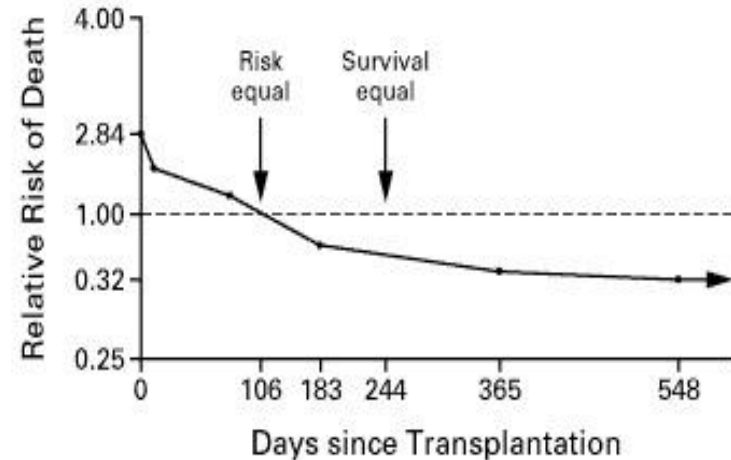


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Kidney Transplant Overview

- ~230,000 patients in US with functioning kidney transplant
- ~91,000 on wait list
- Kidney transplant is preferred means of renal replacement therapy with improved quality and quantity of life versus dialysis.



N Engl J Med. 1999;341(23):172

N Engl J Med. 2021;385:729-43

Kidney Transplant Survival

- Pre-emptive transplant from living donor is ideal
- Patient and allograft survival increasing over past decade

	Live donor	Deceased donor
1 year allograft survival	97.2%	93.4%
5 year allograft survival	84.6%	72.4%
1 year patient survival	98.7%	97.0%
5 year patient survival	93.1%	86.1%

Kidney Allocation

- “Where am I on the wait list?”
- Candidates may accrue time on the kidney transplant wait list once there is a **diagnosis of irreversible kidney disease** and the **GFR is <20mL/min (pre-emptive)** or the **date in which they started dialysis**
- Median wait time for a deceased donor kidney transplant is 4.5 years, but depends on recipient blood type (O and B wait longer), allo-sensitivity and region
- 2014 Kidney allocation system
 - Utilizes **Kidney Donor Profile Index (KDPI)** to predict graft survival and match with Estimated post-transplant survival (EPTS). Lower KDPI is better.
 - Points given for high sensitivity, re-transplant, type B or O blood
 - Back-date of kidney transplant listing to dialysis start date

Overview of Chronic Immunosuppression

- Induction immunosuppression
 - Patients most heavily immunosuppressed 1 year post transplant and at highest risk for opportunistic infections
- Maintenance immunosuppression
 - Standard three drug regimen...
 - **Calcineurin inhibitors** (Tacrolimus and Cyclosporin)
 - Target tacrolimus trough level 5-7 after 1 year
 - Cornerstone of immunosuppressive therapy
 - Nephrotoxic
 - Tacrolimus associated with post-transplant diabetes, neurological toxicity and alopecia.
 - **Prednisone** usually 5mg daily after 1 month post-transplant
 - **Mycophenolate mofetil** 500mg to 1000mg twice per day
 - Teratogenic!
 - Can cause diarrhea (often dose limiting)
 - Reduce dose or stop if opportunistic or serious (i.e. COVID) infection develops

Primary Care of a Kidney Transplant Recipient

- **Opportunistic infections**
 - CMV
 - Highest risk is D+/R- CMV status
 - CMV viremia, viral syndrome, organ invasive disease (bone marrow, kidney, lung, retina, GI tract, liver, pancreas)
 - Treatment: Immunosuppression reduction and anti-viral therapy
 - BK Virus
 - 80-90% seropositive rate
 - Causes chronic tubulo-interstitial nephritis and progressive kidney failure
 - Treatment: Immunosuppression reduction
- **Post-transplant diabetes mellitus (PTDM)**
 - PTDM associated with higher mortality, rejection, CV disease and infection
 - Tacrolimus and prednisone are diabetogenic
 - SGLT-2 inhibitors not rigorously studied in kidney transplant
 - Be careful with metformin due to risk of AKI with kidney transplant

Primary Care of a Kidney Transplant Recipient

- Bone disease
 - Treat residual renal bone disease first
 - Osteoporosis
- Post-transplant malignancy
 - EBV- lymphoma
 - HPV- Cervix, anus, vulva
 - HPV 8, 19 – Squamous cell skin cancer
 - Kaposi sarcoma
 - Native renal cell carcinoma
- Pregnancy
- Immunizations
 - No live-virus vaccines (no intranasal influenza)
 - Shingrix okay

Kidney Transplant and COVID

- COVID immunization
 - Administer vaccination 1-3 months following organ transplant
 - 3rd booster dose at least 28 days following 2nd dose
- Management of COVID infection in transplant recipient
 - For moderate to severe disease, reduce or hold anti-metabolite (MMF)
 - For life-threatening disease hold all immunosuppression except steroids

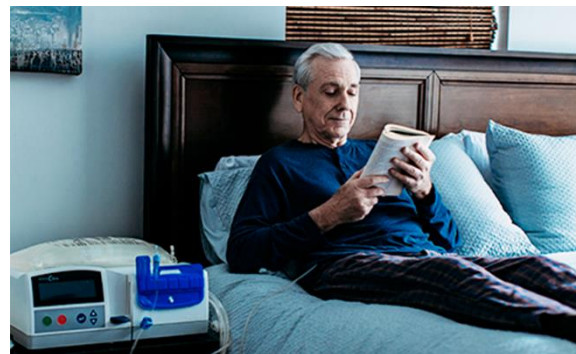
Dialytic Therapies

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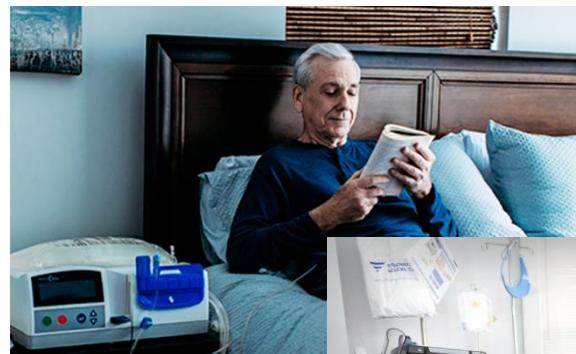
Dialytic Therapies

- Dialytic therapies
 - Peritoneal dialysis
 - Home home dialysis
 - In-center hemodialysis
- Home modality is preferred...
 - Cost savings
 - Possible improved patient outcomes
 - More patient autonomy
 - Improved QOL and less dietary restrictions



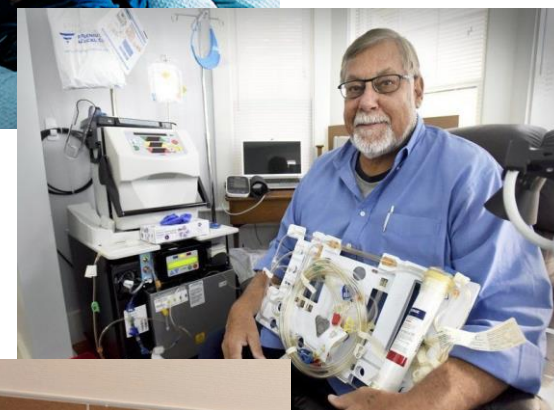
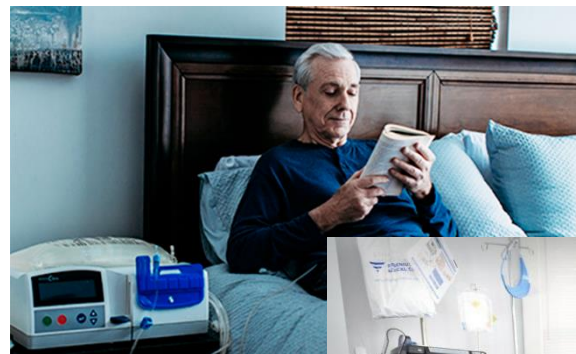
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Peritoneal Dialysis

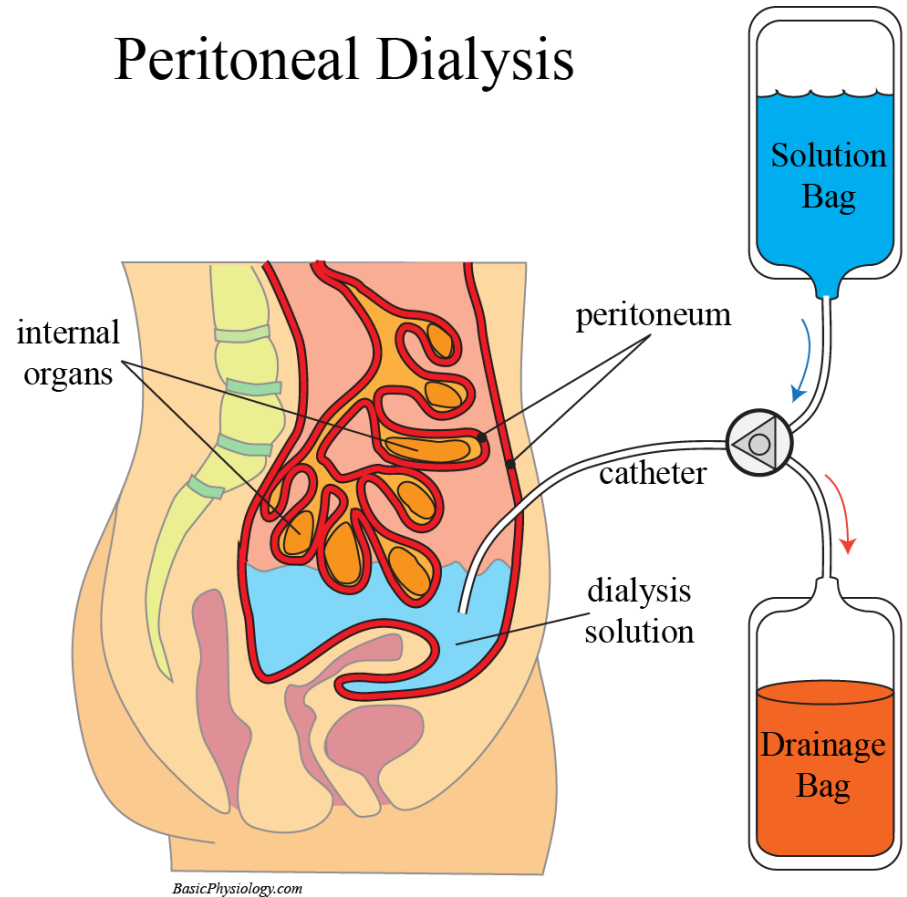
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Peritoneal Dialysis

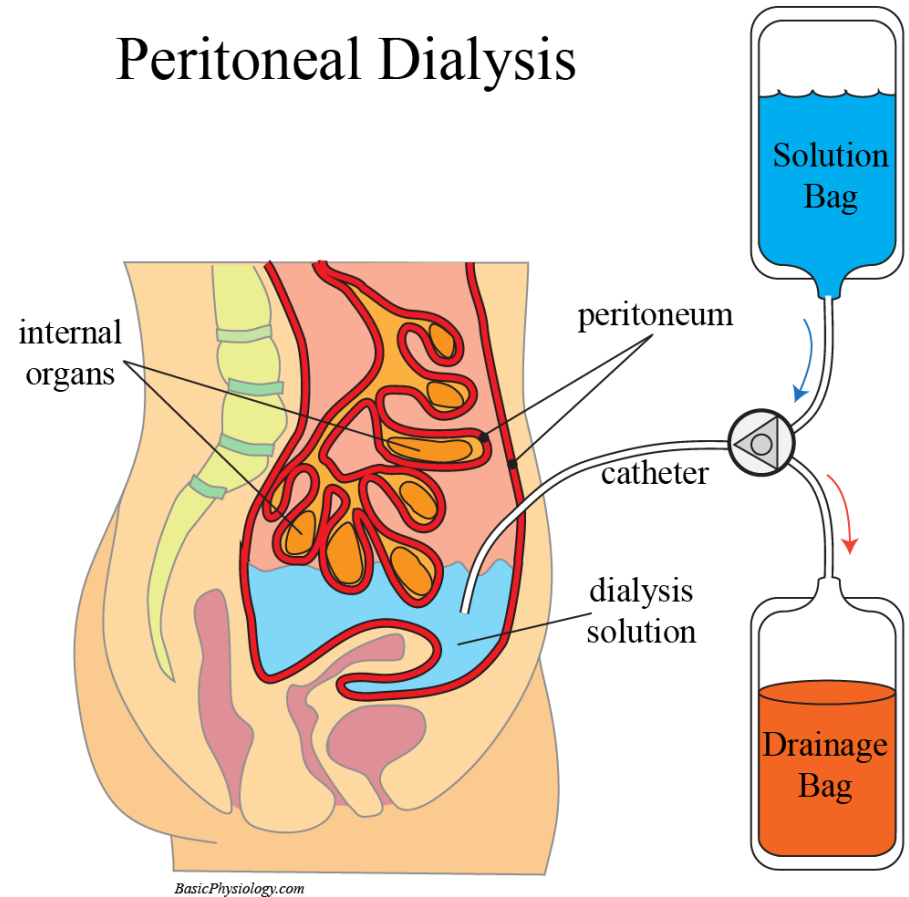
- Peritoneal membrane
- PD solutions
 - Dextrose (1.5%, 2.5%, 4.25%)
 - Icodextran: Decreased absorption, longer osmotic gradient, decreased carb load

Peritoneal Dialysis



Peritoneal Dialysis

- Best for...
 - Younger dialysis patients
 - Advanced heart failure
 - Chronic hypotension
 - Preservation of residual kidney function
- Not good for...
 - Houseless
 - Physically or mentally unable to perform PD (without support)
 - Adhesions/IBD/diverticulitis/ascites/VP shunt
 - Water sports
 - Uncontrolled diabetes (due to dextrose in dialysate)
- Types of PD
 - Continuous ambulatory PD (**CAPD**) – manual, no machine
 - Continuous cycling PD (**CCPD**)- uses machine
 - Buried PD catheter creation at eGFR <15mL/min



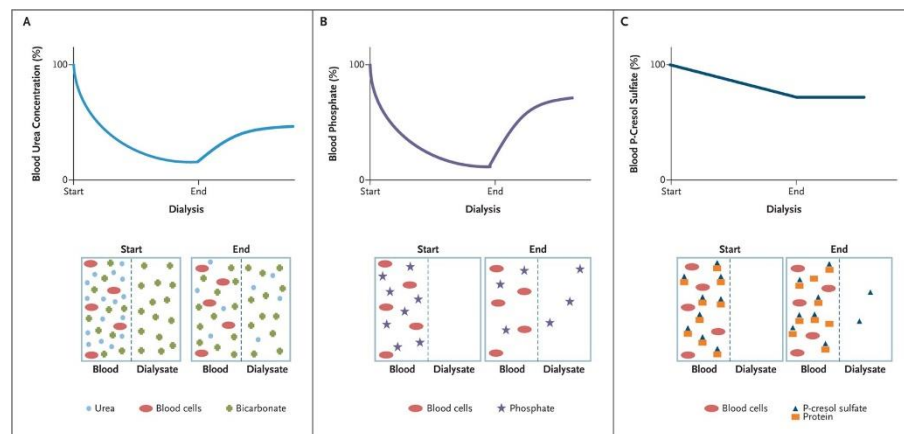
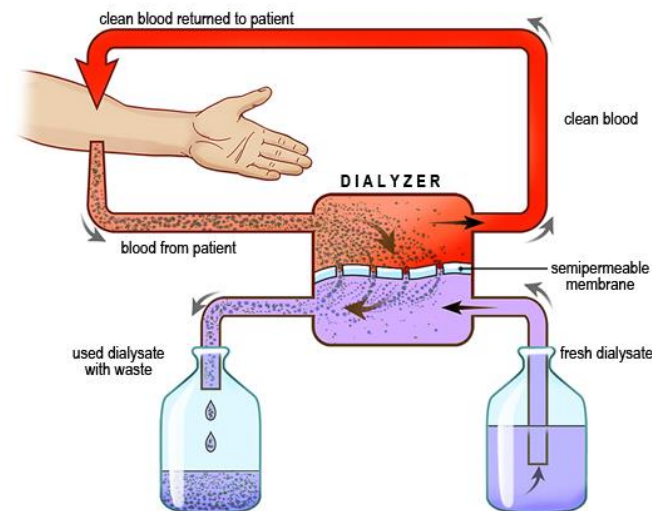
Hemodialysis

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Physiology of Hemodialysis

- Blood and dialysate flow in opposite direction separated by a semi-permeable membrane
- **Diffusion**
- **Convective transport/ultrafiltration**



Hemodialysis. NEJM 201-; 363:1833-1845

Hemodialysis

- Home hemodialysis

- Best for...

- Unable or unwilling to do PD
 - Best overall dialysis outcomes of all modalities

- Not good for..

- Houseless
 - Physically or mentally unable to perform HHD

- Types of HHD

- Conventional (3x/week)
 - Short daily (2-3 hours, 5-7 x/day)
 - Nocturnal (6 nights/week)

- In-center hemodialysis

- Best for...

- Unwilling or unable to home therapy

- 3 days per week, 3-5 hours per session

- Increased risk of sudden death after 2 day interval without HD

Dialysis Modality and Patient Outcome

Dialysis modality	2 year survival (non-DM)	5 year survival (non-DM)
In-center HD	66.8%	42.0%
PD	79%	52.1%
HHD		89.0%

- Data is retrospective and observational
- Patient selection biased
- Randomized controlled trials comparing dialysis modalities and survival have not been done

Cardiovascular Disease in ESRD/Dialysis

- 45% of deaths in dialysis patients due CV disease
- Increased risk of sudden cardiac death in long 2 day interdialytic interval
- Hemodialysis causes myocardial stunning and occult/silent myocardial ischemia.
- Vascular calcifications from altered bone mineral metabolism.
- Questionable role of lipids and statins in primary prevention (AURORA, 4D trials)

AURORA. NEJM 2009;360(14):1395

4D Trial. NEJM 2005;353(3):238

Cardiovascular Disease in ESRD/Dialysis

- Hypertension
 - BP target mid-week, intradialytic BP of $<140/80$
 - Need to control volume and establish accurate “dry weight”
 - Use non-dialyzable anti-hypertensive medications or dose dialyzable anti-hypertensive medications following HD

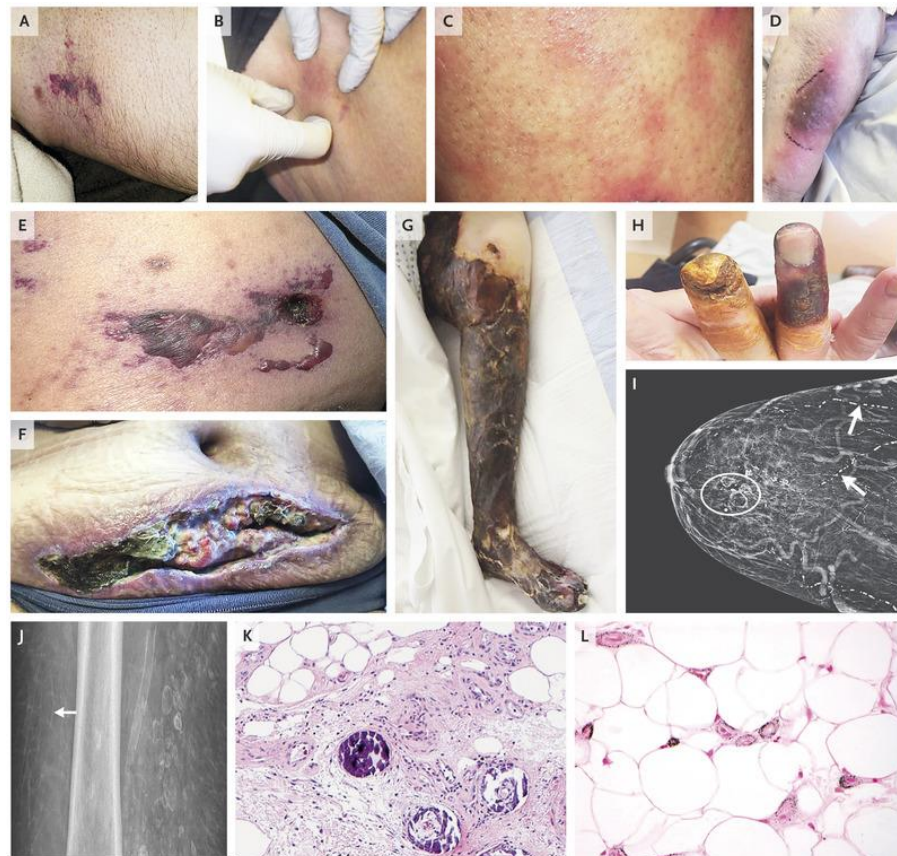
Pharmacokinetics of Antihypertensive Medications in HD

Class/Agent	Dosing	%Removed with HD
Lisinopril	Daily	50%
Fosinopril	Use if intradialytic HTN	Not significant
ARB	Daily	Not significant
Spironolactone	Daily	Not significant
Atenolol	3x/week post-HD	50-75%
Metoprolol	Bid	5-10%
Carvedilol	Bid	Not significant
Labetalol	Bid	<1%
Amlodipine	Daily	Not significant
Clonidine	Bid to tid	5%
Hydralazine	Tid to qid	Not significant

Curr Opin Nephrol Hypertension. 25(3):257-267, 2016

Complication of Dialysis: Calciphylaxes

- Risk factors
 - Severe hyperparathyroidism
 - Over- suppressed iPTH
 - Coumadin
 - Obesity
 - Diabetes
 - > 2 years on dialysis
 - PD > HD
- Therapy
 - Wound care
 - Sodium thiosulfate
 - Avoid vitamin D and calcium
 - Calcimimetics



Calciphylaxes. NEJM 2018; 378:1704-1714

Complications of Peritoneal Dialysis

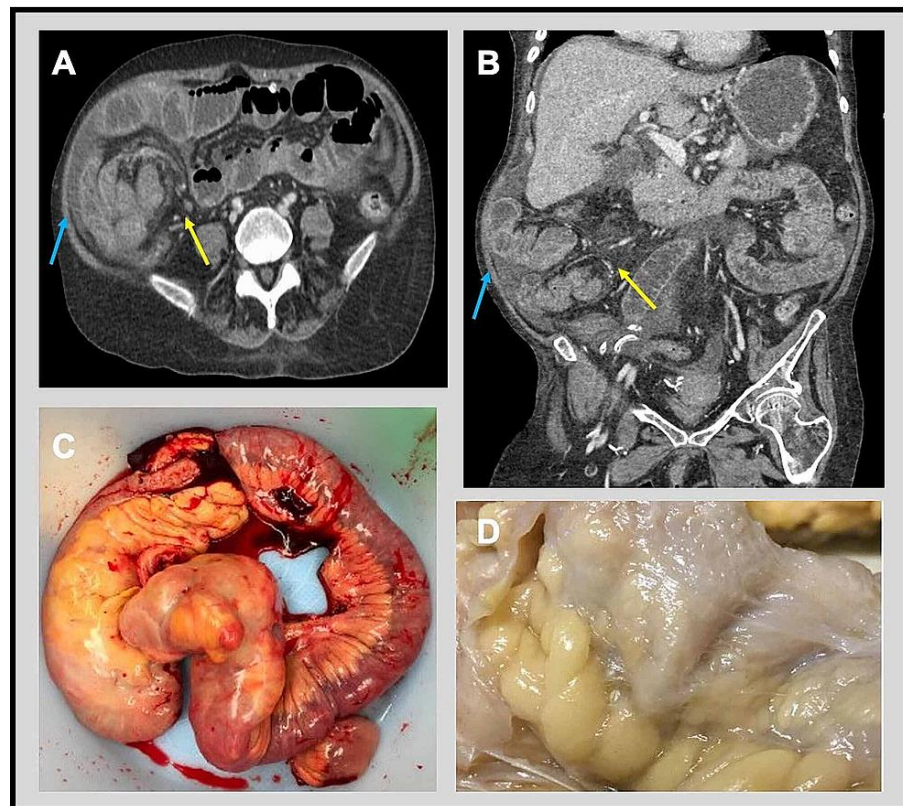
- Peritonitis

- Infectious peritonitis

- Diagnosed with PD fluid cell count of $>100/\mu\text{L}$ and $>50\%$ PMNs
 - Gram positive $>$ gram negative
 - Treat empirically with broad-spectrum IP antibiotics
 - Fungal peritonitis requires removal of PD catheter

- Encapsulating peritoneal sclerosis

- Fibrosis and encasement of bowel
 - Usually occurs >5 years on PD



Dialysis in the Elderly

Supportive Kidney Care (no dialysis)

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Case 1

- 94 year old local Japanese male, 442 Veteran
- Stage 5 CKD, hypertension, mild dementia
- Cr 6.4 (eGFR 7mL/min), BUN 86, K 5.4, CO2 18, Upc ratio 1.3 grams
- Having some mild nausea, itching, metallic taste, decreased appetite



Case 1

- He has been losing weight. He is ambulatory but has an unsteady gait. He has fallen several times in the past month
- He lives in a care home but has a son who visits once per week.



Case 1

- Would you offer renal replacement therapy?
- What is his expected 1 year survival after starting dialysis?
- If renal replacement therapy is selected which modality would you choose?



Case 1

- He would like to live for 8 months until his great granddaughter graduates from high school



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ORIGINAL ARTICLE

Functional Status of Elderly Adults before and after Initiation of Dialysis

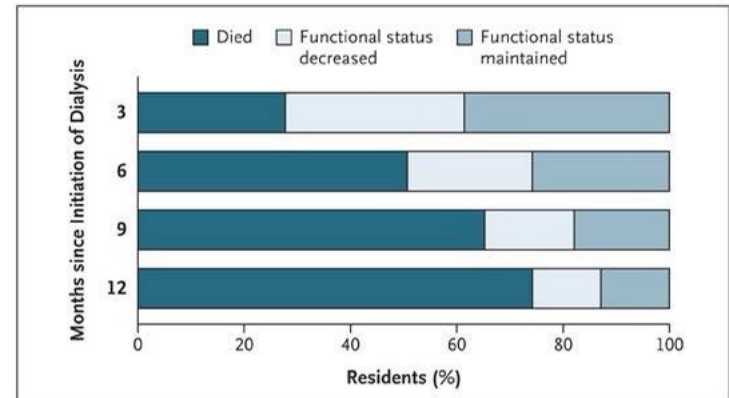
Manjula Kurella Tamura, M.D., M.P.H., Kenneth E. Covinsky, M.D., M.P.H.,
Glenn M. Chertow, M.D., M.P.H., Kristine Yaffe, M.D., C. Seth Landefeld, M.D.,
and Charles E. McCulloch, Ph.D.

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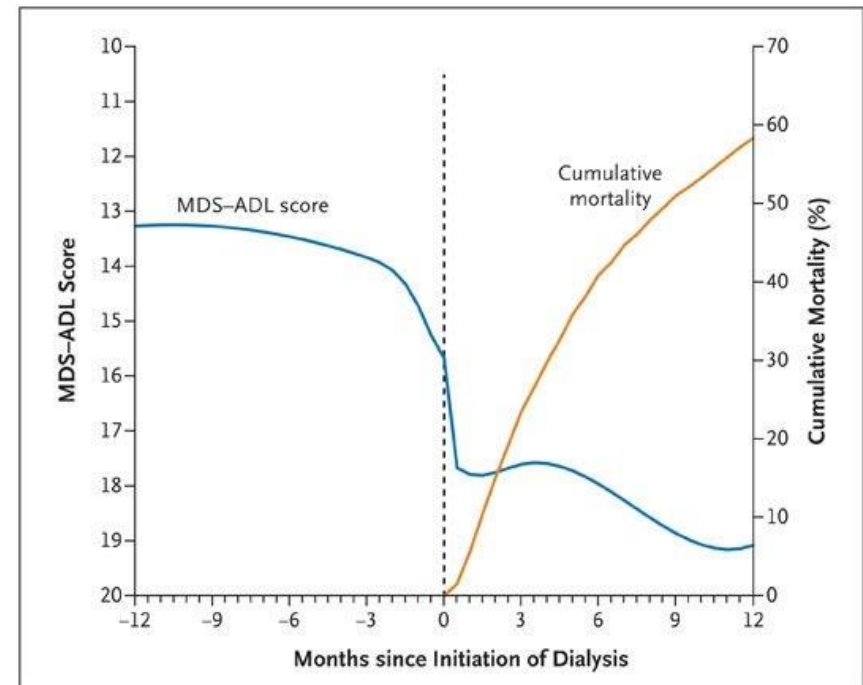
Change in functional status and mortality after initiation of dialysis

- **At 3 months...**
 - 61% had died (26%) or had a decrease in functional status
- **At 6 months...**
 - 78% had died (51%) or had a decrease in functional status
- **At 12 months...**
 - 87% had died (78%) or had a decrease in functional status

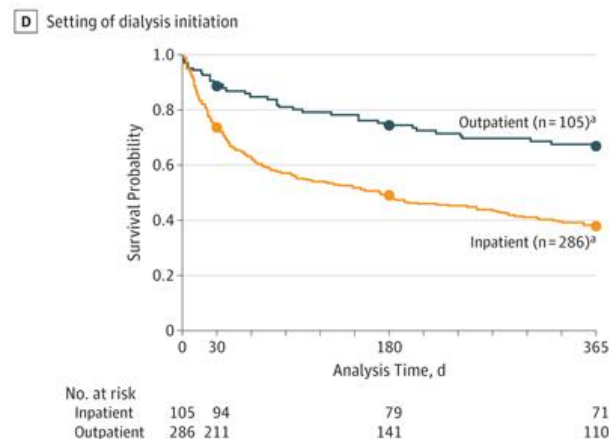
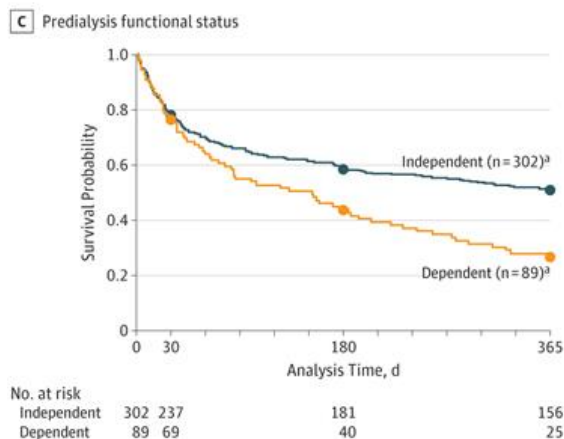
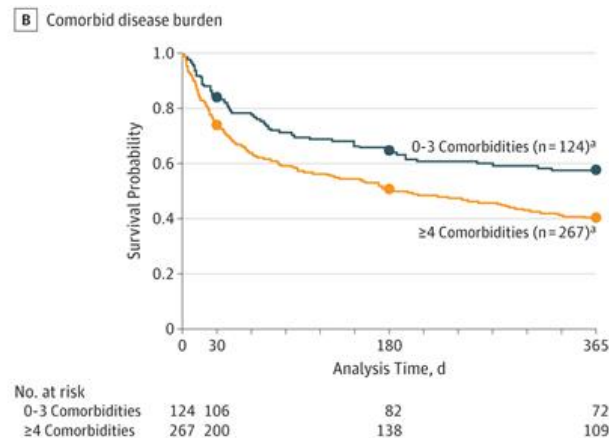
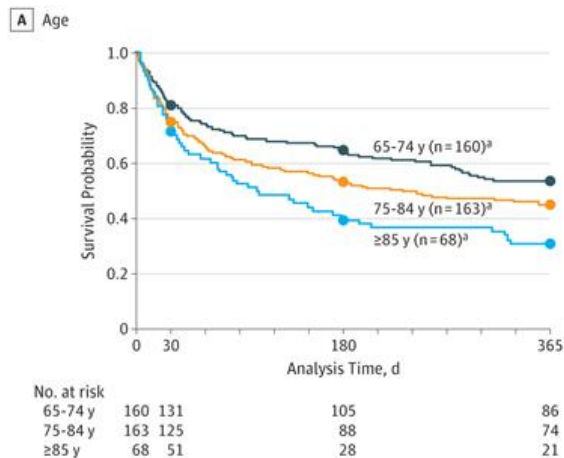


Trajectory of functional status before and after initiation of dialysis

- Average 75 year old nursing home resident
- Dashed line is start of dialysis
- **Conclusion....**
 - Dialysis can preserve life but does not restore health or functional status in elderly nursing home residents



Outcomes of RRT in the elderly (1 Year Mortality After Dialysis Initiation Among Older Adults. JAMA IM. April 2019)



Outcomes of RRT in the elderly (1 Year Mortality After Dialysis Initiation Among Older Adults. JAMA IM. April 2019)

- 22.5% died within 30 days
- 44.2% died within 6 months
- 54.5% died within 1 year
- Poor prognostic indicators
 - Oldest patients
 - Initiation of HD in the hospital
 - High burden of comorbidity

Dialysis versus Conservative Care in Older Adults (CJASN April 2016)

- Single center retrospective survival analysis
- Overall median survival 3.1 years with dialysis, 1.5 years without dialysis
- Survival advantage with dialysis reduced but still statistically significant in patients >70 years
- No survival difference between groups in patients >80 years

Multiple studies show poor outcomes in elderly patients starting dialysis

- **Dismal Rehabilitation in geriatric inner-city hemodialysis patients. JAMA 1994**
 - Initiation of HD does not return elderly patients to previous level of function
- **Effect of age and diagnosis on survival of older patients beginning chronic dialysis. JAMA 1994**
 - Mortality rates increased significantly after initiation of HD with increasing age, no patients >85 years survived more than 5 years on dialysis.
- **Survival outcomes of supportive care versus dialysis therapies for elderly patients with ESKD: A systematic review and meta-analysis. Nephrology 2016**
 - 1 year survival 73% with HD versus 70.6% with supportive care
- **One-year mortality after dialysis initiation among older adults. JAMA International 2019**
 - In patients >65 years starting dialysis, 30 day mortality 22.5%, 44% at 6 months and 54.5% at 1 year

Determinants of Poor Survival

- Physical frailty
- Age over 85
- Poor nutritional status
- Late referral for dialysis
- Inpatient dialysis initiation
- Significant medical co-morbidities (particularly CV disease)

Case 1

- He started in-center hemodialysis. He lived for another year after starting dialysis and was able to see his granddaughter graduate high school. He terminated dialysis several months after her graduation due to progressive functional decline and died several weeks later in hospice care.



Case 2

- 87 year old Korean female
- Stage 5 CKD
- Cr 7.8 (eGFR 5mL/min), BUN 96
- Progressive uremic symptoms
- Lives with elderly husband and physician daughter



Case 2

- Initially, assisted peritoneal dialysis started
 - 1.5L fill volumes
 - 5 exchanges daily
- Patient doing poorly on PD
- Hypotensive, altered, lethargic, poor PO intake



Case 2

- **Assisted PD as an alternative to in-center hemodialysis.**
Brown et. Al. CJASN September 2016
 - Patient satisfaction higher with assisted PD versus in center HD.
 - Similar outcomes (peritonitis, hospitalization rates, mortality).
 - Avoids need to transport to HD unit
 - PD avoids major fluid shifts seen with HD



Case 2

- The patients PD prescription was reduced to 2 manual exchanges per day which was adequate to improve uremic symptoms but without causing hypotension



Case 2: Incremental dialysis

- Okay for shorter, less frequent treatments that do not meet minimal dialysis clearance thresholds but provides enough additional clearance to augment native renal function.
 - Longer preservation of residual renal function
 - Easier on caregivers due to decreased frequency, duration and supplies



Case 3

- 84 year old frail Japanese female
- ESRD from light chain deposition disease
- Severe compression fractures with severe pain during transportation to HD and during in-center HD
- Patient often moaning in pain and shortening HD treatment time due to pain



Case 3

- Patient converted to assisted (granddaughter) home hemodialysis
- Dialyzes at home 2 hours 4 days per week with flexible scheduling
- Appetite, energy and mood improved since converting to home hemodialysis



Case 4

- 76 year old Samoan male
- Stage 5 CKD from diabetic nephropathy, Cr 7.2 (eGFR 7mL/min), BUN 86, K 6.3, CO₂ 12, phosphorus 10.2, Ca 6.2, iPTH 864
- He has itching, dysgeusia and anorexia
- He refuses dialysis



Conservative care of ESRD

- Medical management of ESRD without dialysis or transplant
- Should be considered in patients who may not gain meaningful benefit from renal replacement therapy
- Focus on quality of life
 - **Anemia:** Use ESA therapy to prevent symptomatic anemia
 - **Bone disease:** Avoid painful fracture or symptomatic hypocalcemia or hyperphosphatemia
 - **Metabolic acidosis:** Correcting acidosis can prolong kidney function.
 - **Hyperkalemia:** Prevent symptomatic hyperkalemia or life threatening arrhythmia
 - **Volume overload:** Use diuretics to prevent pulmonary edema or uncomfortable edema
- *Recommendations for Care of Patients Receiving Conservative Kidney Management. CJASN 14: 626-634*

Case 4

- The patient's uremic complications were medically managed with sodium bicarbonate, phos binders, active vitamin D, renal dietary restriction, diuretics, uric acid lowering and ESA therapy
- He survived 5 months and died in home hospice



Conclusions

- Mortality rate in the elderly after starting chronic dialysis is high and <50% are alive after 1 year on dialysis
- Physical function often declines (rapidly) following initiation of chronic dialysis.
- Shared decision making in elderly patients and family with advanced CKD regarding dialysis, including the option for supportive care
- Incremental PD, assisted PD and home hemodialysis are options for elderly patients who elect renal replacement therapy

Future Developments

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Future Developments- TABLO

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Renal Replacement Therapy in Hospitals

Tablo can substantially reduce supply costs and improve labor productivity, freeing you from infrastructure requirements so you can easily dialyze at a patient's bedside, in the ICU, or in the dialysis unit.³

Read our case study: [Cost savings in the Cleveland Clinic ICU](#)



Chronic Care in Dialysis Clinics

Tablo can reduce infrastructure costs and expand the potential locations and configurations of a dialysis clinic, all while creating a meaningfully better experience for patients.

► Watch video: [Empowering dialysis patients with in-center self-care](#)



Home Dialysis

Tablo's user friendly interface, quick training, simple setup, and sensor-based automation make home hemodialysis an easy, efficient, and flexible option for chronic dialysis patients.

Review our home clinical trial results: [Safety and efficacy of the Tablo hemodialysis system for in-center and home hemodialysis](#)

Future Developments- TABLO

- Benefits of TABLO
 - Unifies and consolidates dialytic care across all spectrums of care (acute, ICU, in-center, home).
 - No central water treatment infrastructure needed
 - Simplified iPad-like user interface, faster training for staff and patients
- Concerns
 - Low dialysate flow rate (50-300mL/min versus 600-800mL/min) may lead to inadequate clearance
 - Cross training of non-dialysis staff to be TABLO dialysis staff

Tablo.

TOUCHSCREEN GUIDANCE

Animations and conversational instructions make Tablo easy to learn and use

TABLO CARTRIDGE

Minimizes setup and takedown time by removing manual steps

DIALYSATE ON DEMAND

Purifies water and produces dialysate in real-time

SENSOR-BASED AUTOMATION

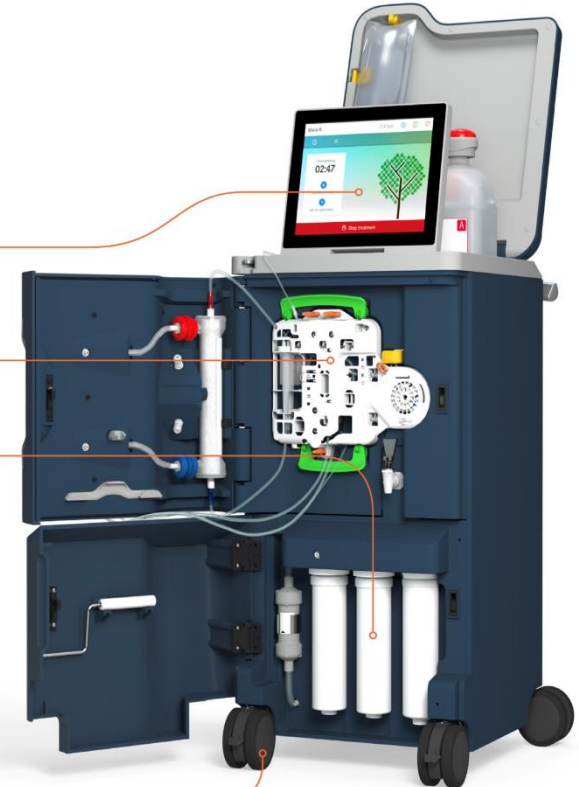
Tablo sensors help to automate much of the setup, treatment management and maintenance

WIRELESS CONNECTIVITY

Two-way data communication can automatically send treatment data to the cloud

MOBILITY

All you need is an electrical outlet and tap water



“iPhonization” of the Dialysis Industry



Future Developments – Xenotransplant

- Genetically altered pig kidney externally attached to a brain dead patient
- Kidney worked immediately and functioned normally, making urine and excreting creatinine
- Tracked for 54 hours with no signs of acute rejection

The New York Times

In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked

A kidney grown in a genetically altered pig functions normally, scientists reported. The procedure may open the door to a renewable source of desperately needed organs.



Dr. Robert Montgomery is director of the N.Y.U. Langone Transplant Institute in Manhattan. Genetically engineered pigs “could potentially be a sustainable, renewable source of organs,” he said. Amir Hamja for The New York Times

New York Times October 19, 2021

Conclusions

- Kidney transplant is the preferred means of renal replacement therapy
- Dialytic therapies include peritoneal dialysis, home hemodialysis and traditional in-center hemodialysis
- Home therapies are preferred over in-center HD
- Goals of care discussion should be had with elderly CKD patients including the option for renal supportive care without dialysis
- Tablo is a promising new dialytic technology

Q&A

CREATING A HEALTHIER HAWAI'I

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Thank you!

- A recording of the meeting will be available afterwards.
- Unanswered question?
 - Contact us at info@hawaiihealthpartners.org