AJKDblog.org

NephMadness.com

This will re-direct to the Tourneytopia bracket site
If it's March, it's time for NephMadness

1. Register at NephMadness.com
2. Read Scouting Reports at AJKDblog.org
3. Make your picks at NephMadness.com
4. Submit brackets from March 13 – April 3

Cheer for your teams
Debate your friends
@NephMadness
@AJKDonline
#NephMadness

AJKDblog.org

Free CME • Free MOC

8 experts hand picked
32 nephrology concepts
1 crazy month of learning
Bracket submission March 13 - April 3
- Earn MOC and CME credits
- Open to individuals and/or groups
- Details available at AJKDblog.org
- Free to enter
Fill out your bracket

31 decisions

2,147,483,648 possible bracket combinations
Winners decided by votes from Blue Ribbon Panel

- Kirk Campbell @kirkcAMPbell
- Richard Knight @knightra
- Vandana Niyyar @vandyniyyar
- Holly Kramer @kramer_holly
- Kimberly Manning @gradydoctor
- Magdalena Madero @MagdelenaMadero
- Jessica Reid-Adams @DoctorJRA
- Roger Rodby @NephRodby
- Mark Rosenberg @roseym24

Their instructions: “For each matchup, pick the team that you think will cause the most practice change in Nephrology over the next 5 years.”
Hyperkalemia
K Binders in CKD
## K Binders in CKD

<table>
<thead>
<tr>
<th></th>
<th>Sodium Zirconium Cyclosilicate (Lokelma)</th>
<th>Patiomer (Veltesa)</th>
<th>Sodium Polystyrene Sulfonate (Kayexalate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>$K^+ \rightleftharpoons Na^+ &amp; H^+$</td>
<td>$Ca^{2+} \rightleftharpoons K^+$</td>
<td>$Na^+ \rightleftharpoons K^+$ exchange resin</td>
</tr>
<tr>
<td>Duration</td>
<td>1 hour</td>
<td>7 hours</td>
<td>Hours to Days</td>
</tr>
<tr>
<td>Location</td>
<td>Entire GI tract</td>
<td>Colon</td>
<td>Colon</td>
</tr>
<tr>
<td>Side Effects</td>
<td>Edema, GI Drug interference</td>
<td>GI ↓sMg^{2+} Drug Interference</td>
<td>Colonic necrosis, Hypernatremia, Metabolic alkalosis, Edema Drug interference</td>
</tr>
<tr>
<td>Cost</td>
<td>$700</td>
<td>$850</td>
<td>$40</td>
</tr>
</tbody>
</table>
SPS and the risk of GI side effects
Is the use of sodium polystyrene sulfonate (SPS) associated with a higher risk of hospitalization for adverse GI events?

**Methods and Cohort**
- Ontario, Canada
- Retrospective matched cohort
- Adults > 65 years
- April 2003 – March 2016

**Exposure**
- First outpatient prescription for SPS
- 20,020 Rx
- 30 day follow up

**GI adverse events**
- HR: 1.94 (1.10-3.41)
- 23 per 1000 person-years
- vs
- 18 per 1000 person-years

**Conclusions** The use of sodium polystyrene sulfonate is associated with a higher risk of hospitalization for serious adverse GI events. These findings require confirmation and suggest caution with the ongoing use of sodium polystyrene sulfonate.

Patiromer lowered potassium in a large RCT and kept it down for 52 weeks
AMETHYST-DN: Does patiromer work in patients with hyperkalemia and diabetes?

### Methods and cohort
- **Phase 2 RCT**
  - Open label, dose-ranging
- **48 sites**
  - 5 European countries
- **Type 2 diabetics**
  - n = 306
- **eGFR 15 - <60**
  - Serum K >5.0
- **RAAS inhibition**
  - Prior to and during study

### Primary efficacy end point
- **Mean change in serum K level**
  - Baseline to week 4 or prior to dose titration
  - **Mild hyperkalemia**
    - 5.1 – 5.5
    - Daily dose: 8.4 g
    - Decrease in K: 0.35
    - Daily dose: 16.8 g
    - Decrease in K: 0.51
    - Daily dose: 25.2 g
    - Decrease in K: 0.55
  - **Moderate hyperkalemia**
    - 5.6 – 5.9
    - Daily dose: 16.8 g
    - Decrease in K: 0.87
    - Daily dose: 25.2 g
    - Decrease in K: 0.97
    - Daily dose: 33.6 g
    - Decrease in K: 0.92

### Primary safety end point
- **Adverse events**
  - Through 52 weeks
  - **Mg²⁺**
    - 7.2%
    - Hypomagnesemia
  - **Constipation**
    - 6.3%
  - **Hypokalemia (<3.5)**
    - 5.6%

### Secondary efficacy end point
- **Mean change in serum K level**
  - Through 52 weeks
  - **Statistically significant decrease in serum K at each monthly point**

### Conclusions
Among patients with hyperkalemia and diabetic kidney disease, patiromer starting doses of 4.2 to 16.8 g twice daily resulted in statistically significant decreases in serum potassium level after 4 weeks of treatment, lasting through 52 weeks.

These binders are well tolerated and allow the use of drugs that would normally be stopped or not started due to worries of hyperkalemia.
Can Patiromer enable spironolactone use in patients with resistant hypertension and CKD?

**Phase 2 Trial**
- 62 Outpatient Centers
- 10 Countries
- n= 295
- eGFR 25 to ≤ 45
- Uncontrolled Resistant Hypertension
- K = 4.3 to 5.1 mmol/L

**Primary Outcome**
- Remained on Spiro
- 86%
- Change in SBP
- -11.7 (-14.1 to -9.3)
  - From base line p< 0.001

**Secondary Outcome**
- Change in SBP
- 19.5%
  - Dif: 19.5%
  - p<0.0001
- Change in SBP
- -10.8 (-13.2 to -8.3)
  - From base line p< 0.001

**Run In Period**
- 8.4g Patiromer o.d.
- + 25mg Spironolactone
- + Baseline Medication
- n=147

**Dose titration**
- >1w: Patiromer
- >3w: Spironolactone
- n=148

**Placebo**
- + 25mg Spironolactone
- + Baseline Medication

**Conclusions**
In patients with resistant hypertension and chronic kidney disease, patiromer enabled more patients to continue treatment with spironolactone with less hyperkalaemia. Persistent spironolactone enablement in this population of patients has clinical relevance for the treatment of resistant hypertension.

VA by Verner Venegas
K is Good in CKD
K is Good in CKD

Diets high in potassium are associated with:
- Lower blood pressure
- Reduced risk of cardiovascular mortality
- Reduced Risk of stroke

Diets high in potassium tend to have more alkali:
- Less kidney stones
- Less progression of CKD
Diets low in potassium were associated with more development of CKD
Does sodium and potassium intake play a role in the development of chronic kidney disease (CKD) in the general population?

**Prevention of Renal and Vascular End-Stage Disease (PREVEND) study**

- 25-75 years
- No CKD at baseline

**Definition of CKD**

- De novo development of eGFR < 60 mL/min/1.73m²
- Albuminuria > 30 mgs/24 hours

872 patients developed CKD (median 10.3 years)

**Baseline urine sodium**

135 mmol/24 hours (IQR: 106-169)

**Baseline urine potassium**

70 mmol/24 hours (IQR: 57-85)

**No association was observed between urine sodium and risk of CKD**

**Each 21 mmol/day decrease in urine potassium was associated with a 16% higher risk of developing CKD**

HR 1.16 (1.06-1.28)

**Conclusion**

Low potassium excretion (and not high urine sodium) was associated with an increased risk of developing CKD in a population-based cohort with normal kidney function.


Visual Abstract by Edgar Lerma, MD, FASN
Addition of fruits and vegetables or alkali slowed progression of CKD stage 3. There was no difference in serum potassium
Does treatment of metabolic acidosis with diet or bicarbonate therapy affect CKD progression?

**Randomization**
- Stage 3 CKD
- $\text{TCO}_2$ 22-24 mmol/L
- 3 years follow up
- $n = 108$

**Usual Care**
- Plasma $\text{TCO}_2$
- Urine Angiotensinogen

**NaHCO$_3$ or Base-producing fruits & vegetables**
- (Designed to reduce dietary acid load by 50%)

**Conclusion**
Dietary alkali treatment of metabolic acidosis in CKD that is less severe than that for which KDOQI recommends therapy reduces kidney angiotensin II activity and preserves eGFR.


Visual Abstract by Edgar Lerma, MD, FASN
K Binders in CKD

K is Good in CKD

pick one
Exercise Causes HyperK
Exercise Causes HyperK

Following muscle depolarization, potassium leaves the myocyte through voltage gated potassium channels to repolarize the cell.

This can cause hyperkalemia.

During vigorous exercise, muscle extracellular potassium can increase by more than 3 mmol/L.
Exercise Prevents HyperK
Exercise Prevents HyperK

- Muscle is the primary buffer against increases in potassium
- Insulin resistance decreases the ability to buffer potassium
- Exercise that increases muscle mass and decreases insulin resistance has the potential to protect against hyperkalemia
11 patients on dialysis

60 minutes of exercise after dialysis

3 months

Pre-dialysis potassium went from 5.2 to 4.5
Exercise Causes HyperK

Exercise Prevents HyperK

pick one
Now pick your Hyperkalemia Champion
HD Access
Percutaneous AVF Creation
Percutaneous AVF Creation

Anastomoses are created between the radial or ulnar artery and a deep vein of the forearm that mature into the AVF.

Patient selection is important.

Two techniques: WavelinQ and Ellipsys:
- WavelinQ: Utilizes fluoroscopy, two magnetic catheters, and radiofrequency energy to create the anastomosis.
- Ellipsys: Utilizes ultrasound, one catheter, and thermal energy to create the anastomosis.
## Percutaneous AVF Creation

Technical success rate and patency rate of percutaneous AVF creation in different trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Technical success rate</th>
<th>Patency rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WavelinQ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rajan et al (FLEX)</td>
<td>2015</td>
<td>97%</td>
<td>96.5% at 6 months</td>
</tr>
<tr>
<td>Lok et al (NEAT)</td>
<td>2017</td>
<td>98%</td>
<td>84% at 12 months</td>
</tr>
<tr>
<td>Radosa et al</td>
<td>2017</td>
<td>100%</td>
<td>100% at 6 months</td>
</tr>
<tr>
<td>Berland et al</td>
<td>2019</td>
<td>100%</td>
<td>78% at 6 months</td>
</tr>
<tr>
<td><strong>Ellipsys</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hull et al</td>
<td>2016</td>
<td>88%</td>
<td>87% at 6 weeks</td>
</tr>
<tr>
<td>Hull et al</td>
<td>2017</td>
<td>95%</td>
<td>92% at 1 year</td>
</tr>
<tr>
<td>Mallios et al</td>
<td>2018</td>
<td>97%</td>
<td>94% at last follow up (max 6 months)</td>
</tr>
<tr>
<td>Beathard et al</td>
<td>2019</td>
<td>98%</td>
<td>92% at 24 months</td>
</tr>
</tbody>
</table>
Surgical AVF Creation
Surgical AVF Creation

Has been around since 1960

Allows for more sites than the pAVFs.
- Surgical ingenuity has led to AVF with the axillary femoral, popliteal, and even the dorsalis pedis arteries!

Years of long term data available (not available with pAVF) showing durability

Unassisted failure to mature is an issue in as many as 50-60% of AVF
Percutaneous AVF Creation

Surgical AVF Creation

pick one
EU Guidelines
EU Guidelines

42 pages with 32 guidelines

Suggests regional block anesthesia over general anesthesia for AVF surgery

No recommendations on catheters

Use the rope-ladder or buttonhole technique for AVFs with choice dependent on local expertise and AVF characteristics

Slide 38 discusses differences in pharmacotherapy recommendations for maintaining the access
American Guidelines
164 pages with 26 guidelines

Includes the ESKD-LIFE plan

Suggests tunneled CVCs are acceptable for short or even long term in certain situations

Anesthesia: operators discretion

Use rope-ladder over buttonholes
<table>
<thead>
<tr>
<th>Intervention</th>
<th>European</th>
<th>American</th>
</tr>
</thead>
<tbody>
<tr>
<td>For Early/AV access maturation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>2C; Balance risk of bleeding versus benefit when on monotherapy, do not stop</td>
<td>Suggests not using clopidogrel monotherapy to improve maturation and prevent primary failure (10.5)</td>
</tr>
<tr>
<td>Fish Oil for AVG</td>
<td>2C; Balance benefit of increased patency against unknown risk of bleeding</td>
<td>Suggest use of oral fish oil for newly created AVG to reduce patient morbidity (14.6)</td>
</tr>
<tr>
<td>Exercise</td>
<td>2C; Suggest using hand and arm exercises to improve maturation</td>
<td>Inadequate evidence for recommending upper arm exercise</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence to recommend specific exercises</td>
<td>Recommend use of whole arm rather than finger exercises (10.3)</td>
</tr>
<tr>
<td>Infrared therapy</td>
<td>2C; balance benefit of decreased thrombosis against uncertain benefit on maturation and risk of bleeding</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Late/to maintain AV access patency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish oil for AVF</td>
<td>2C; Balance benefit of increased patency at 1 year against increased risk of bleeding</td>
<td>Suggest not using fish oil for AVF (14.2)</td>
</tr>
<tr>
<td>Fish oil for AVG</td>
<td>2C; Balance benefit of increased patency against unknown risk of bleeding</td>
<td>Insufficient evidence to recommend fish oil to prolong cumulative patency (14.7)</td>
</tr>
<tr>
<td>Infrared therapy for AVF</td>
<td>2C; consider using for improving long term patency</td>
<td>Suggest use should be based on individual circumstances, feasibility, and judgment (14.1)</td>
</tr>
<tr>
<td>Warfarin for AVG</td>
<td>1C; against using warfarin with other antiplatelets OR clopidogrel with aspirin</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Antiplatelets for AVF/AVG</td>
<td>Insufficient evidence</td>
<td>Suggest not using aspirin for AV (14.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suggest careful consideration of combination aspirin + dipyridamole (14.5)</td>
</tr>
</tbody>
</table>
EU Guidelines

pick one

US Guidelines
Now pick your HD Access Champion

Percutaneous AVF Creation

Surgical AVF Creation

EU Guidelines

US Guidelines
Vaccines
Flu Vaccine
Flu Vaccine

- Flu vaccine results in decreased rates of mortality
  - 25% on HD
  - 34% on PD
- ~71% of patients on HD get a flu vaccine
- Seroconversion is LOWER in patients on HD
  - 81% in general population vs. 47% on dialysis
- How can Seroconversion be improved?
What About High Dose Vaccine?

Is high dose influenza vaccine more effective than the standard dose in patients on dialysis?

<table>
<thead>
<tr>
<th>Methods</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>USRDS observational</td>
<td>Standard dose</td>
<td>All cause mortality: 8.7% 1st hospitalization for influenza/pneumonia: 7.6% Influenza like illness: 28.1%</td>
</tr>
<tr>
<td>Patients included</td>
<td>High dose</td>
<td>Risk difference (SDV vs HDV): Risk difference (SDV vs HDV)</td>
</tr>
<tr>
<td>&gt;65 years N = 225,215</td>
<td>n=507,552</td>
<td>9.3% 9.2% 30.0%</td>
</tr>
</tbody>
</table>
What about adding an Adjuvant?

• The presence of the adjuvant
  • MF59 (oil-in-water emulsion of squalene oil)
  • improves the immune response to the flu vaccine.

• Study of 169 patients on HD from Korea (~56 yrs old)
  • MF59-adjuvanted vaccines demonstrated better immunogenicity (compared to standard dose)
  • Has NOT been studied in regards to diminishing hospitalizations etc.

• Current approach is to continue vaccination with standard flu vaccination
Pneumonia Vaccine

- 1 in 5 (21%) of patients develop pneumonia within a year of starting dialysis

- In the following 6-month period AFTER pneumonia diagnosis
  - Mortality
    - HD with pneumonia 73 per 100 patient-years
    - HD no pneumonia 15 per 100 patient-years
  - Thus, we NEED to do a better job with pneumococcal vaccination
Rates of pneumococcal are lower than flu vaccine

- Data from NHANES, CDC, ARIC Study

Ishigami et al AJKD July 2019
There are currently two approved pneumococcal vaccines:

1. Prevnar 13 or PCV13 which contains 13 different pneumococcal serotypes;
2. Pneumovax 23 or PPSV23 which contains an additional 11 serotypes.

Current strategy is to use BOTH.
Survival according to flu and pneumococcal vaccination status

- 36,966 patients (US ESRD Network 6) on PD and HD who had been on dialysis for greater than 1 year and with known vaccination status

Bond et al AJKD December 2012
Flu Vaccine

Pneumonia Vaccine

pick one
Live Vaccines in Transplant
# Live Vaccines in Transplant

Danziger-Isakov et al AJT March 2013

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended Before Transplant</th>
<th>Recommended After Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus Calmette–Guérin</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Measles Mumps Rubella</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Smallpox</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Varicella- Zostavax</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Varicella- Zarivax</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>
Live Vaccines in Transplant

- The use of *live* vaccines in transplantation is controversial.

- They have been listed as *contraindicated*
  - risk of causing disseminated disease from immunosuppressed state.

- reemergence of measles, mumps, varicella

- Is it time to reconsider in patients who are not vaccinated

- Especially if outbreak develops

- Highlights need to get these before transplant

measles data from WHO
**Measles Cases Surpass 700 as Outbreak Continues Unabated**

The outbreak is now the worst in decades. Children under age 5 account for about half of the cases.

By Donald G. McNeil Jr.

April 30, 2019

Measles continues to spread in the United States, federal health officials said on Monday, surpassing 700 cases this year as health officials around the country sought aggressive action to stem the worst outbreak in decades.
What is the risk of live vaccines in transplantation?

Are live vaccines safe in immunocompromised patients?

**Methods and Cohort**
- Systematic review 64 articles
- Immunosuppression
- Solid organ transplant
- Bone marrow transplant

**Intervention**
- n = 20556
- n = 339
- n = 187
- Herpes zoster
- MMR
- Varicella
- Yellow fever

**Outcomes**
- **Vaccine-related infections**
  - 12 (0.06%)
  - 16 (4.7%)
  - 4 (2.13%)
- 11 SAE from vaccine reactions
- Variable immunogenicity
- High risk of bias

**Conclusions** Although live vaccinations were safe and sufficiently immunogenic in most studies, some serious reactions and vaccine-related infections were reported. Until further data are available live vaccinations should only be given after careful risk benefit assessment.

No Live Vaccines in Transplant
No Live Vaccines in Transplant

- The mantra of **Team No Live Vaccines in Transplant**
  - “risks of disease dissemination caused directly by the vaccine is far worse than the immunity that it would potentially confer”
  - Thus, we should avoid live vaccines at all costs

- Although we are seeing a resurgence in measles and mumps
  - only occurring in isolated clusters
  - The current risk/benefit ratio
    - **risk** when it comes to Live Vaccines.
Timing of Vaccines after Immunosuppression Induction

- Delay for 6 months post induction or B cell depletion
  - Low effectiveness

- Influenza vaccine is exception to the rule
  - 1 month delay if pandemic
  - 3 month if transplant occurs during flu season

- In 2017, the FDA approved Shingrix to prevent zoster in adults $\geq 50$
  - non-live recombinant subunit vaccine
  - first zoster vaccine that could be given while immunocompromised.
# No Live Vaccines in Transplant

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended Before Transplant</th>
<th>Recommended After Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Human Papilloma Virus</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Inactivated Polio</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Influenza</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Pertussis</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Pneumococcal (PCV13 and PPSV23)</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Tetanus</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Varicella - Shingrix</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

Danziger-Isakov et al AJT March 2013
Is non live adjuvanted recombinant zoster vaccine (RZV) effective in adults following kidney transplant?

**Background**
- Herpes Zoster 9x more frequent in organ transplant recipients.
- Non live adjuvanted RZV in adult post kidney transplant recipients (KTx) studied.

**Methods**
- Phase 3, Observer-Blind, Randomized (1:1) Multi Center Trial
- n=264
- 2 Doses of RZV / Placebo
- 1-2 months apart in 4-18 months post KTx

**Results**
- **Humoral and cell-mediated immune responses** higher in RZV cohort.
- Immunity persistent across time points for 12 months after last dose.

**Immune Monitoring**
- Anti-glycoprotein E (gE) Antibody Concentration.
- gE Specific CD 4-T Cell Frequency.
- Vaccine Response Rate.

**Conclusions**: Non live RZV was immunogenic in chronic immunosuppressed kidney transplant recipients. Immunogenicity persisted through 12 months post vaccination. No safety concerns were reported.


Visual Abstract by Dr. Krishnam Raju Penmatsa
@krishnadoc1
Live Vaccines in Transplant

No Live Vaccines in Transplant

pick one
Now pick your Vaccines Champion

Flu Vaccine
Live Vaccines in Transplant

Pneumonia Vaccine
No Live Vaccines in Transplant
Ethics
Policy-Driven Outcomes for Dialysis
Policy-Driven Outcomes for Dialysis

Beneficence - moral imperative that actions must promote collective well-being.

Currently, 88% of ESKD patients in the US receive in-center HD

PD benefits - preserves residual kidney function, less infections
Home HD benefits - improved cardiac structure, better nutritional parameters

Both home options are cost-saving when compared to in-center HD
Policy-Driven Outcomes for Dialysis

Kidney Health Initiative (KHI) introduced in July 2019, aims for 80% of patients with ESKD to obtain a transplant or be maintained on a home dialysis modality by 2025.

Financial incentives being put in place to minimize the discordance between the desire to initiate/maintain home options for patients vs actual incidence of utilization.
Patient-Driven Choice For Dialysis
Patient-Driven Choice For Dialysis

Autonomy - allows for individuals to make decisions that align with their moral framework without coercion from others

Influences that may factor into decisions of dialysis - age, income, desire for travel, functional status, life goals, cultural beliefs, social support, comorbid conditions, depression, caregiver dependence, etc.

Financial incentives pushing for home dialysis options infringe on shared-decision making and impact patient’s autonomy
What are the nephrologist perceived barriers to chronic peritoneal dialysis utilization in USA?

**Background**
- Steep decline in patients with ESKD on PD
- 33% Nephrologist aspired PD utilization.

**Methods**
- Questionnaire sent to medical directors of dialysis centers across New England
- n=117

**Results**
- 50% Medical directors responded.
- 29% Nephrologists *desired* PD prevalence.
- 15% Patients with ESKD *actually* on PD in New England.

**Expectations?**
- ?

**Limitations?**
- ?

**Concerns?**
- ?

**Barriers**
- 54% Patient Preference
- 32% Medical Contraindications
- 31% Poor Social Support

**Concerns**
- 25% Technique Failure
- 25% Long term Viability of PD
- 17% Mortality Rates of PD

**Conclusions**: Nephrologist desired vs actual incidence of PD in New England is 29% vs 15% respectively. Main factors limiting PD utilization are patient choices, medical contraindications and poor social support. Major concerns of nephrologists were technique failure and long term viability of PD. Focus on these domains is vital for PD survival in USA.


Visual Abstract by Krishnam Raju Penmatsa

@krishnadoctort1
Policy-Driven Outcomes for Dialysis

Patient-Driven Choice for Dialysis
End-of-Life Care for Patients on Dialysis
End-of-Life Care for Patients on Dialysis

Nonmaleficence - primum non nocere, “first do no harm”

Continuing/offering dialysis support for those at end-of-life may be prolonging suffering, causing harm

Voluntary withdrawal of dialysis is #3 cause of death in patients receiving dialysis (after CV and infection)
End-of-Life Care for Patients on Dialysis

RPA/ASN Guidelines suggesting that dialysis be withdrawn or withheld for the following:

- those with decision-making capacity who refuse dialysis
- those without decision-making capacity who have previously indicated a desire for refusal in oral or written advance directive
- those without decision-making capacity whose legal surrogate refuses dialysis
- those with irreversible neurologic impairment
- those whose medical condition precludes the technicalities of the procedure (eg profound hemodynamic instability)

- those with Stage V CKD older than 75 who have two of the following:
  - nephrologist would not be surprised if patient were to die within a year
  - High comorbidity score
  - Impaired functional status
  - Severe malnutrition
Dialysis for Patients at End-of-Life
Dialysis for Patients at End-of-Life

Justice - fairness in medical decisions, equal distribution of resources

ESKD is officially a hospice-appropriate diagnosis, yet Medicare only provides hospice coverage for patients with a terminal illness unrelated to kidney disease.

→ Patients for whom ESKD is the terminal illness must stop dialysis prior to receiving Medicare coverage for hospice care.
**What is the association between hospice length of stay and end-of-life health care utilization and costs among patients on HD?**

<table>
<thead>
<tr>
<th>METHODS</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>USRDS</td>
<td></td>
</tr>
<tr>
<td>Hospice duration</td>
<td></td>
</tr>
<tr>
<td>n=770,191</td>
<td></td>
</tr>
<tr>
<td>Not enrolled</td>
<td></td>
</tr>
<tr>
<td>Hospital admission</td>
<td>74.4%</td>
</tr>
<tr>
<td>ICU admission</td>
<td>51.0%</td>
</tr>
<tr>
<td>Intensive procedure</td>
<td>31.6%</td>
</tr>
<tr>
<td>Died in hospital</td>
<td>55.1%</td>
</tr>
<tr>
<td>Cost for last week of life</td>
<td>&gt;$10k</td>
</tr>
<tr>
<td>Treated with HD</td>
<td></td>
</tr>
<tr>
<td>&lt;3 days to death</td>
<td></td>
</tr>
<tr>
<td>Hospital admission</td>
<td>83.6%</td>
</tr>
<tr>
<td>ICU admission</td>
<td>54.0%</td>
</tr>
<tr>
<td>Intensive procedure</td>
<td>17.7%</td>
</tr>
<tr>
<td>Died in hospital</td>
<td>13.5%</td>
</tr>
<tr>
<td>Cost for last week of life</td>
<td>&gt;$10k</td>
</tr>
<tr>
<td>&gt;15 days to death</td>
<td></td>
</tr>
<tr>
<td>Hospital admission</td>
<td>35.1%</td>
</tr>
<tr>
<td>ICU admission</td>
<td>16.7%</td>
</tr>
<tr>
<td>Intensive procedure</td>
<td>3.0%</td>
</tr>
<tr>
<td>Died in hospital</td>
<td>5%</td>
</tr>
<tr>
<td>Cost for last week of life</td>
<td>&lt;$4k</td>
</tr>
</tbody>
</table>

**CONCLUSION:** Hospice referral among patients on HD occurs very late in the course of illness as an add-on to intensive patterns of care. Measures to improve hospice access and integrate palliative care in patients on HD are needed to bring meaningful changes in patterns of health care utilization, costs, and quality of end-of-life care in the ESKD population.

Melissa W. Wachterman, Susan M. Hailpern, Nancy L. Keating, Manjula Kurella Tamura, Ann M. O’Hare Association Between Hospice Length of Stay, Health Care Utilization, and Medicare Costs at the End of Life Among Patients Who Received Maintenance Hemodialysis JAMA Intern Med. 2018;178(6):792-799

Visual abstract by Krithika Mohan, MD.
End-of-Life Care for Patients on Dialysis

Dialysis for Patients at End-of-Life
Now pick your Ethics Champion

Policy-Driven Outcomes for Dialysis

Patient-Driven Choice for Dialysis

End-of-Life Care for Patients on Dialysis

Dialysis for Patients at End-of-Life
Green Nephrology
Climate Change and AKI
Climate Change and AKI

Mean global temperature increase of 0.8° C over past 50 years

Increase in natural disasters, heat waves, water shortages

Direct AKI - nephrolithiasis, heat stroke

Indirect AKI - increased vector-borne diseases
  - Malaria (1-5% of patients develop AKI)
  - Dengue (11-36%)
Climate Change and CKD
Climate Change and CKD

Epidemic of CKDu described in sugarcane workers in central America.

Also seen in brickmakers in Nicaragua, where 30% of workers at one factory had CKD5, and 22% were younger than age 35!

Combination of heat leading to hypovolemia, dehydration, hyperosmolarity, and potentially concentration of nephrotoxin leading to this.
Decline in Kidney Function in Young Adults at Risk of Mesoamerican Nephropathy

Methods

Community based Cohort study Nicaragua

n = 263
87
350

Data Collected:

- Questionnaire
- Clinical Measures
- Blood & Urine tests

6 monthly visits, over 2 years

eGFR Trajectories in men (n = 263)

Rapid Decline in eGFR:

-18 ml
/min/1.73m²/yr

9.5% n = 25

(β = -14 ml/min/1.73m²/yr; n = 3)

Baseline kidney dysfunction:

-3.8 ml
/min/1.73m²/yr

9.5% n = 25

(β = no patients met this criteria)

Preserved & Stable eGFR:

-0.6 ml
/min/1.73m²/yr

81% n = 213

(β = -0.6 ml/min/1.73m²/yr; n = 84)

Associations with Rapid Decline in eGFR

Primary Analysis

- Lack of shade OR - 3.74
  95% CI, 1.59 to 8.76
- Outdoor Work OR - 10.35
  95% CI, 1.35 to 79.24
- Agricultural work OR - 3.57
  95% CI, 1.14 to 11.13

Sensitivity analysis

- Sugarcane Cutting OR - 3.84
  95% CI, 1.17 to 12.58
- Fever (last 6 mths) OR - 5.77
  95% CI, 2.03 to 16.33

Conclusion: Although, Mesoamerican nephropathy is associated with agricultural work, other factors may also contribute to this disease. A subset of patients showed rapid decline in renal function.


VA by: @aakashshingda
Climate Change and AKI

Climate Change and CKD
Consumable Waste in HD
Consumable Waste in HD

Running dialysate at 800 ml/min, how much water is consumed in a 3 hour treatment?

144L of dialysate required, but remember that source water goes through filtration, deionizer, reverse osmosis, which consumes an additional 240L.

Factor in priming, rinsing, and sterilization of each treatment, total use of over 500L of water per treatment!

Power is another resource! 2 HD treatments consume enough power to last an average 4-person home or one whole week.
“Reject water” can be reused for flushing, landscaping, groundskeeping, etc.

Solar power can eventually break net-even, but takes several years. Still an important consideration in areas with limited power.
Disposable Waste in HD
Disposable Waste in HD

Average American produces 2 kg of garbage/day

Each HD treatment produces 2.5 kg of waste, 38% of which is PLASTIC

Even PD creates 1.69 kg of waste/day - ends up being more than HD per week!

Majority of waste is PC, which is disposed of via incineration
Disposable Waste in HD SOLUTIONS

Segregate biohazardous waste at the source, which allows for recycling and reduced disposal costs. This is already enforced in UK.

Repurposing rather than incineration. Trials underway to shred plastic and incorporate into concrete for waterproofing effect.
Consumable Waste in HD

Disposable Waste in HD

pick one
Now pick your Green Nephrology Champion
Biomarkers in Rejection
Biomarkers in Rejection

- The allograft biopsy, serum creatinine, and proteinuria have traditionally been used to identify patients with kidney transplant rejection - with significant limitations.

- Below are a few players that have been able to NON-INVASIVELY detect rejection in the kidney transplant:

  - Urine chemokines (CXCL8, CXCL9, CXCL10)
  - Donor-derived cell-free DNA (*Donor DNA circulating in the recipient*)
  - Blood + urine mRNA (Single genes, gene signatures)
  - Interferon γ ELISPOT (Recipient’s donor-reactive T-cells)
Is the use of CXCL9 validated as a risk-stratifying biomarker for kidney transplant injury?

<table>
<thead>
<tr>
<th>Methods</th>
<th>Association with AR</th>
<th>Results &amp; outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First transplant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTOT-01 protocol</td>
<td>CXCL9 mRNA, CXCL9 protein, Granzyme B</td>
<td><strong>CXCL9</strong></td>
</tr>
<tr>
<td>Multicenter N=280</td>
<td><strong>≥Banff 1A acute rejection</strong></td>
<td>PPV: 67.6% NPV: 92.0%</td>
</tr>
<tr>
<td><strong>Biopsy</strong></td>
<td>CXCL10, CCR1, CXCR3, IL-8</td>
<td></td>
</tr>
<tr>
<td><strong>Urine biomarkers</strong></td>
<td>Creatinine &amp; GFR</td>
<td></td>
</tr>
<tr>
<td><strong>Conclusion</strong>: Low urinary CXCL9 levels post kidney transplant is associated with low acute immunological risk and can exclude acute rejection/infection. It may have a role as a valuable biomarker in identifying patients destined to display stable long-term allograft function.</td>
<td>D. E. Hricik, P. Nickerson, R. N. Formica, E. D. Poggio, D. Rush, K. A. Newell, J. Goebel, I. W. Gibson, R. L. Fairchild, M. Riggs, K. Spain, D. Ike, N. D. Bridges, P. S. Heeger for the CTOT-01 consortium Multicenter Validation of Urinary CXCL9 as a Risk-Stratifying Biomarker for Kidney Transplant Injury Am J Transplant,13 (10), 2634-4413 (10) VA by Krithika Mohan, MD.</td>
<td></td>
</tr>
</tbody>
</table>
Biopsy in Rejection
Biopsy in Rejection

- The allograft biopsy is the gold standard for diagnosis of kidney transplant rejection - though complications, cost, sampling bias and interpretation remain a challenge.

- Below are two emerging strategies to enhance our use of biopsy tissue:
  - Microarray ("Molecular Microscope", tissue RNA expression)
  - Computer-Assisted & Machine Learning Techniques
Can gene transcripts predict kidney allograft failure before fibrosis occurs?

GoCAR study
Prospective, multicenter

Protocol allograft kidney biopsies at 3 months
n = 204

Stable kidney function
3 months post-transplant

Microarray analysis
(3 month sample)
Investigating gene transcript expression

Identify gene transcripts
Correlating with Chronic Allograft Damage Index (CADI) score at 12m

13 gene transcripts
Independently predicted development of fibrosis at 1 year (CADI-12 ≥ 2)

High predictive capacity
(AUC 0.967)
Compared to:
Baseline clinical variables (AUC 0.706)
Clinical & pathological variables (AUC 0.806)

Helps discriminate high vs low risk of progression
(AUC 0.916)

Predictive value validated
Independent cohort in GoCAR (n=45, AUC 0.866)
Independent publicly available datasets (n=282, AUC 0.831 and n=24, AUC 0.972)

Predicts early allograft loss
Loss at 2 years (AUC 0.842)
Loss at 3 years (AUC 0.844)

Conclusions This set of 13 gene transcripts could be used to identify kidney transplant recipients at risk of allograft loss before the development of irreversible damage, thus allowing therapy to be modified to prevent progression to fibrosis.


Visual abstract by Michelle Lim, MBChB, MRCP
Can we perform histologic analysis in kidney tissue through a deep learning framework?

**Training & Validation (A)**
- 40 whole-slide images (WSI)
- 71 fully annotated regions

**Applications**
- Glomerular segmentation & detection (D)
- Correlation Banff components (E)
- 15 whole-slide Images (WSI)
- 82 biopsies

**Average Dice Coefficient**
(measures how similar a set and another set are)

0.88

**Highest performance for glomeruli, tubuli & interstitium segmentation**

**Equal performance on external center**

**CNN-based quantifications correlate significantly between visually scored histologic components of the Banff scoring system.**

**Conclusions:** This is the first validation of quantitative results obtained by a convolutional neural network (CNN) with components of the Banff classification system. The results of these analyses are encouraging for the application of deep learning in kidney (transplantation) pathology.

Biomarkers in Rejection

Biopsy in Rejection

pick one
Marijuana OK
Marijuana OK

- Marijuana use is legal in several states, and has the potential to provide benefits to our patients with various symptoms (i.e. anxiety, depression, insomnia, nausea, pruritus)

- Existing (but limited) data show that marijuana use in either donors or recipients does not significantly impact allograft function

- Activation of the cannabinoid receptor may be immunomodulatory

- Inclusion of marijuana-using donors may expand the living donor pool
Marijuana Users Had Similar Allograft Survival Compared to Non-Users

Should donors who have used marijuana be considered candidates for living kidney donation?

**Methods and Cohort**
- Single academic institution
- Retrospective review
- Living kidney transplants
  - Jan 2000 – May 2016
  - Marijuana-using: n = 31
  - Non-marijuana-using: n = 163

**Outcomes**
- No difference in donor or recipient perioperative characteristics
  - \( P > 0.05 \) All comparisons
- No difference in postoperative outcomes
- No difference in kidney function between marijuana users and non-users
- No long-term difference in kidney allograft function between marijuana-user donors and non-users

**Conclusion**
Considering individuals with a history of marijuana use for living kidney donation could increase the donor pool and yield acceptable outcomes.

Marijuana Not OK
Marijuana Not OK

- Marijuana potency has increased over the past 20 years, and use can lead to “cannabis use disorder” or even addiction.

- Marijuana use has been described to impair executive function, concentration, and attention - raising concerns for immunosuppressant non-adherence.

- Cannabidiol is an inhibitor of cytochrome P450 isoform CYP3A and thus can directly impact calcineurin inhibitor (CNI) levels.
Marijuana Not OK

- “Cannabis arteritis” has been described and may lead to increased platelet aggregation and vasospasm.
- Marijuana users demonstrate higher rates of cigarette smoking and increased consumption of alcohol, sodium, pork, cheese, and salty snacks.
- Marijuana use may increase rates of fungal infection in patients with kidney transplants.
Marijuana OK

pick one

Marijuana Not OK
Now pick your Transplant Champion

Marijuana OK

Marijuana Not OK
Women With X-linked Alport
Women With X-linked Alport

Caused by mutations in the gene COL4A5 encoding the alpha 5 chain of type IV collagen.

NOT a carrier state!

Disease severity based upon lyonization of the X-chromosome

15-30% of women develop ESRD

Kidney biopsy, genetic testing, or skin biopsy can help diagnose.
Immunofluorescence microscopy in women with X-linked Alport syndrome can show a mosaic pattern of alpha 5 (IV) staining consistent with random X-inactivation. Red: alpha 2 (IV), Green: alpha 5 (IV) (Image courtesy of Dr. Michelle Rheault, University of Minnesota Masonic Children's Hospital)
Autosomal Dominant Alport
Heterozygous for COL4A3 or COL4A4
-But NOT just thin basement membrane disease

Responsible for a significant portion of patients with FSGS and steroid resistant nephrotic syndrome

<table>
<thead>
<tr>
<th>Risk Factors for CKD Progression in ADAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
</tr>
<tr>
<td>Family history of kidney disease</td>
</tr>
<tr>
<td>progression and ESKD</td>
</tr>
<tr>
<td>FSGS</td>
</tr>
<tr>
<td>GBM thickening and lamellation</td>
</tr>
</tbody>
</table>
Autosomal Dominant Alport Syndrome

What pathogenic mutations are identified in a cohort of patients with FSGS?

Methods and Cohort

- Wessex Kidney Centre
  - n = 81; 79 Caucasian
- Primary FSGS or SRNS
  - 80 FSGS: 73 biopsy-proven
  - 1 SRNS
- Targeted Next Generation Sequencing
  - 39 genes on panel

Outcomes

- Mutation Identification Rate
  - 13% Definitely pathogenic
  - 20% Definitely or probably pathogenic

By Age

- Adult: 20%
- Adolescent: 14%
- Child: 33%

Gene Mutation Identified

- 4/22 NPHP4
- 2/22 COL4A3
- 1/22 COL4A4
- 4/22 NPHS1
- 2/22 INF2
- 2/22 COL4A5
- 7/22 Other

Conclusions

Using a targeted next-generation sequencing panel in a cohort of patients with FSGS in England, collagen IV mutations were found to frequently underlie FSGS.

Reference:
VA by @Stones__
Women With X-linked Alport

pick one

Autosomal Dominant Alport Syndrome
Genetic Counseling for Stones
## Genetic Counseling for Stones

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene Mutations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystinuria</td>
<td>SLC3A1, SLC7A9</td>
<td>Urine alkalinization, cystine-binding medications, reduce sodium intake</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and animal protein intake</td>
</tr>
<tr>
<td>Primary hyperoxaluria</td>
<td>AGXT, GRHPR, HOGA1</td>
<td>Depending on mutation liver transplant, pyridoxine, reduced</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydroxyproline intake</td>
</tr>
<tr>
<td>Distal renal tubular acidosis</td>
<td>SLC4A1, ATP6V1B1, ATP6V0A4, FOXI1</td>
<td>Potassium citrate, thiazide diuretics</td>
</tr>
<tr>
<td>Dent disease</td>
<td>CLCN5, ORCL</td>
<td>Thiazide diuretics, reduce sodium intake</td>
</tr>
</tbody>
</table>

Summary of some of the most common monogenic causes of kidney stones
Genetic Counseling for Cystic Diseases
Consider genetic testing for cystic kidney disease in children with early onset or aggressive disease.

Next generation sequencing for PKD1, PKD2, PKHD1, DZIP1L, and HNF1B

One study found pathogenic mutations in 78% of patients undergoing genetic testing.

Both positive and negative tests can cause significant psychological distress.
Genetic Counseling for Cystic Diseases

How can a kidney gene panel be used to reveal the diagnosis in suspected inherited kidney disease?

**Methods and Cohort**
- Barcelona, Spain 2014 - 2016
- Suspected cystic or glomerular inherited kidney disease
- Validation Cohort
  - Previously Known Mutation: n = 116
- Diagnostic Cohort
  - Suspected Inherited Kidney Disease: n = 421

**140-kidney gene panel**
- Identified Pathogenic Mutation: 115/116
- Cystic: 161/207
- Glomerular: 61/98

**Conclusions**
In a Spanish cohort of 421 patients with suspected cystic or glomerular inherited kidney disease, a 140-gene panel revealed the genetic diagnosis in 78% of patients with suspected cystic and 62% of patients with suspected glomerular inherited kidney disease.

**Suspected Inherited Kidney Disease**
- Cystic
  - Diagnosis Confirmed: 62%
  - New Diagnosis: 14%
  - Diagnosis Changed: 2%
  - No Mutation Identified: 22%
- Glomerular
  - Diagnosis Confirmed: 57%
  - New Diagnosis: 5%
  - Diagnosis Changed: 1%
  - No Mutation Identified: 37%

Genetic Counseling for Stones

pick one

Genetic Counseling for Cystic Diseases
Now pick your Genetics Champion
TG Feedback

Hyperglycemia increases activity of the sodium glucose transporter in the proximal tubule.

More Na reabsorption leads to increased BP.

More Na reabsorption means less Na (and Cl) delivered to the macula densa (MD).

The MD interprets the drop in Na (and Cl) as decreased flow to the glomerulus and compensates by causing afferent arteriolar vasodilation.

This causes hyperfiltration.
Hyperglycemia leads to decreased delivery of chloride to the macula densa. This results in increased glucose, Na, and Cl reabsorption at the proximal tubule, leading to an increased glomerular filtration rate (GFR) and intra-glomerular pressure, which is referred to as hyperfiltration.
SGLT2 block this hyperfiltration

By stopping the sodium glucose transporter, hyperglycemia no longer increases Na resorption

Now there is too much sodium delivered to the macula densa.

This is interpreted as too much flow to the glomerulus and TG feed back causes afferent arteriole vasoconstriction

The vasoconstriction lowers glomerular blood pressure and reverses hyperfiltration
macula densa detects **increased** delivery of chloride

CONSTRUCT

Decreased GFR
Decreased intra-glomerular pressure

**correction of hyperfiltration**
So the next time you see the small bump in creatinine when you start an SGLT2i, think that is the medications way of telling you, “It’s working”
Non-TG Feedback
Non-TG Feedback

TG feedback is cool but it can’t explain the improvement in heart failure and total mortality, there must be something else going on.

SGLT2i are anti-inflammatory

They decrease oxygen consumption in the proximal tubule

They switch the primary fuel from free fatty acids to more efficient beta-hydroxybutyrate

Anti-fibrotic action
If afferent arteriolar constriction was the secret to fighting diabetic kidney disease we would be passing out ibuprofen to all of our CKD patients.
TG Feedback

pick one

Non-TG Feedback
SGLT2i in Transplant
Many concerns about UTI

Bumps in creatinine

Increased risk of volume depletion

Unclear benefits in this population
Is empagliflozin (SGLT2i) safe and efficient in kidney transplant recipients (KTR) with PTDM?

Methods and Cohort
- Prospective Single Center Double-Blind
- Post-transplant Diabetes Mellitus (PTDM)
- > 1 year post KTR
- Stable eGFR > 30 ml/min/1.73m²
- Stable Immunosuppression

n = 49

Intervention
- Empagliflozin 10mg
- Placebo

n = 49

Intervention
- n = 24
- Empagliflozin 10mg
- n = 25
- Placebo

Outcomes
- HbA₁c
  - After 24 Weeks on treatment
  - ∆HbA₁c: -0.2% p = 0.025
  - If > 8% HbA₁c ∆HbA₁c: -1.0%

Greater reduction if eGFR > 60

Weight
- Mean 24h Arterial Blood Pressure
- Uric Acid
- Hemoglobin

- Weight: -2.5 kg p = 0.014
- Mean 24h Arterial Blood Pressure: n/s p = 0.85
- Uric Acid: -53 umol/L p < 0.01
- Hemoglobin: 0.45 g/dL p = 0.047

2 patients with repeated urinary tract infections and urosepsis

Conclusions
Empagliflozin appeared safe and improved glycemic control in renal transplant recipients with PTDM compared with placebo. A concomitant reduction in body weight was seen. Concerns regarding UTIs remain.


Visual Abstract by Verner Venegas.
SGLT2i Without DM
The SGLT2i are not good anti-diabetic drugs with A1c dropping by only 0.3-0.5

But despite that they dramatically reduce kidney and heart failure outcomes.

Maybe you don’t even need diabetes to see a benefit from these drugs
SGLT2i Without DM

In DAPA-HF 60% of patients did not have diabetes,

Despite that, dapagliflozin reduced heart failure by 25% compared to a placebo

EMPA-Kidney is now enrolling patients and we should see results by 2022.

Primary outcome is progression of CKD, dialysis, or CV death.

Patients do not need to have diabetes to be enrolled
SGLT2i in Transplant

pick
one

SGLT2i Without DM
Now pick your SGLT2i Champion

SGLT2i in Transplant

SGLT2i Without DM
From your Effluent Eight teams, pick your Filtered Four:
From your Filtered Four teams, pick your Left and Right Kidneys…

…as you only need 1 kidney, put your Champion below:
Thanks for playing!

Participate in the social media discussion:

#NephMadness