THE KIDNEY, FOR THE LONG TERM: AKI and LONG TERM CARE

Samuel Snyder, D.O.
snyderdo@nova.edu
Outline

• Kidney function and aging: what are we measuring?
  • The healthy aging kidney
  • The aging kidney that is also failing
  • The acutely failing kidney

• AKI in the elderly
  • Risk factors
  • Recognition
  • Role of polypharmacy
  • Treatment and outcome

• Bonus: BP – How high is too high?
Measuring kidney function
Creatinine clearance (mL/min) = 
\[
\frac{(140 - \text{age [years]}) \times \text{weight [kg]}}{\text{serum creatinine [\mu mol/L]}} \quad \text{(Females)}
\]
\[
(140 - \text{age [years]}) \times \text{weight [kg]} \times 1.2 \quad \text{(Males)}
\]

serum creatinine [\mu mol/L]
### Table 46. Estimating GFR in Adults

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Equation/Sample</th>
<th>No. of Subjects* (Measurements)</th>
<th>GFR Range (ml/min/1.73 m²)</th>
<th>Accuracy** 30% 50% Blase (%)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levin, 2007</td>
<td>1,773</td>
<td></td>
<td>94 94 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levy, 2006</td>
<td>1,673/655</td>
<td></td>
<td>85 83 23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ban corrected (GFR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rollin, 1994</td>
<td>354 (506)</td>
<td></td>
<td>74 91 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toto, 1997</td>
<td>100</td>
<td></td>
<td>78 96 –14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamm, 1993</td>
<td>Diabetes</td>
<td>136</td>
<td>77 92 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy &amp; stone throwers</td>
<td>110</td>
<td></td>
<td>96 100 –3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlton, 1993</td>
<td>100</td>
<td></td>
<td>66 84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waller, 1991</td>
<td>171</td>
<td></td>
<td>81 94 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Della 1991</td>
<td>124</td>
<td></td>
<td>70 85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy</td>
<td>62</td>
<td></td>
<td>80 80 –5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sault, 1992</td>
<td>100 (197)</td>
<td></td>
<td>70 92 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedros, 1990</td>
<td>321 (786)</td>
<td></td>
<td>66 84 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scint, 1997</td>
<td>127 (142)</td>
<td></td>
<td>56 85 25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Cockcroft-Gault equation is:

\[
\text{GFR (ml/min)} = \frac{(140 - \text{Age}) \times \text{Weight (kg)}}{72 \times \text{SCr}^{1.15}}
\]

Markers for measuring GFR include:


* When multiple measurements were made for each subject, the total number of measurements appears in parentheses.

* Accuracy defined as the percent of GFR estimates within 30% or 50% of measured GFR.

* See Part 10, Appendix 3 for definition of bias.

* Cockcroft-Gault equation standardized for 1.73 m² body surface area.

* Bias correction utilized a multiplier which corrected the overall bias of the development set to 0. The bias noted is calculated from the validation (test) set when available.

* 1,070 subjects in model development set; 558 subjects in validation set.

* Percent of estimates within 35% of the true value.

* Bias is rough estimate from the graph.

Abbreviations: CKD, chronic kidney disease; CG, Cockcroft-Gault Equation, BSA, body surface area
<table>
<thead>
<tr>
<th>Name</th>
<th>Patient Type</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cockcroft-Gault</td>
<td>All</td>
<td>$C_F = \frac{((140 - \text{age}) \times \text{weight})}{(72 \times S_{Cr}) \times 0.85}$ (if patient is female)</td>
</tr>
<tr>
<td>MDRD</td>
<td>All</td>
<td>$\text{GFR} = 186 \times (S_{Cr})^{-1.154} \times \text{(age)}^{-0.203} \times 0.742$ (if patient is female) or $\times 1.212$ (if patient is black)</td>
</tr>
<tr>
<td>MDRD adjusted</td>
<td>All</td>
<td>$\text{GFR} = 175 \times (\text{standardized } S_{Cr})^{-1.154} \times \text{(age)}^{-0.203} \times 0.742$ (if patient is female) or $\times 1.212$ (if patient is black)</td>
</tr>
<tr>
<td>CKD-EPI</td>
<td>Women: Creatinine level $\leq 0.7 \text{ mg/dL}$</td>
<td>$e\text{GFR} = 144 \times (S_{Cr}/0.7)^{0.329} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>White women</td>
<td>$e\text{GFR} = 144 \times (S_{Cr}/0.7)^{0.329} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Black women</td>
<td>$e\text{GFR} = 166 \times (S_{Cr}/0.7)^{0.329} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Women: Creatinine level $&gt; 0.7 \text{ mg/dL}$</td>
<td>$e\text{GFR} = 144 \times (S_{Cr}/0.7)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>White women</td>
<td>$e\text{GFR} = 144 \times (S_{Cr}/0.7)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Black women</td>
<td>$e\text{GFR} = 166 \times (S_{Cr}/0.7)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Men: Creatinine level $\leq 0.9 \text{ mg/dL}$</td>
<td>$e\text{GFR} = 141 \times (S_{Cr}/0.9)^{0.411} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>White men</td>
<td>$e\text{GFR} = 141 \times (S_{Cr}/0.9)^{0.411} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Black men</td>
<td>$e\text{GFR} = 163 \times (S_{Cr}/0.9)^{0.411} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Women: Creatinine level $&gt; 0.9 \text{ mg/dL}$</td>
<td>$e\text{GFR} = 141 \times (S_{Cr}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>White men</td>
<td>$e\text{GFR} = 141 \times (S_{Cr}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td></td>
<td>Black men</td>
<td>$e\text{GFR} = 163 \times (S_{Cr}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$</td>
</tr>
<tr>
<td>Cystatin C¹¹</td>
<td>Cystatin C alone</td>
<td>$\text{eGFR} = 76.7 \times (\text{cystatin C})^{-1.18}$</td>
</tr>
<tr>
<td></td>
<td>CKD-EPI Cystatin</td>
<td>$\text{eGFR} = 127.7 \times (\text{cystatin C})^{-1.17} \times (\text{age})^{-0.13} \times (0.91$ if patient is female) $\times (1.06$ if patient is black)</td>
</tr>
<tr>
<td></td>
<td>Combined cystatin C and creatinine</td>
<td>$\text{eGFR} = 177.6 \times (\text{creatinine})^{0.65} \times (\text{cystatin C in mg/L})^{-0.57} \times (\text{age})^{-0.20} \times (0.82$ if patient is female) $\times (1.11$ if patient is black)</td>
</tr>
<tr>
<td>Berlin Initiative Study (BIS)¹⁵</td>
<td>Creatinine alone</td>
<td>$\text{eGFR} = 3736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95} \times 0.82$ (if female)</td>
</tr>
<tr>
<td></td>
<td>Combined cystatin C and creatinine</td>
<td>$\text{eGFR} = 767 \times (\text{creatinine})^{-0.61} \times \text{creatinine}^{-0.40} \times \text{age}^{-0.57} \times 0.87$ (if female)</td>
</tr>
</tbody>
</table>

Comparison to $^{125}$I-Iothalamate GFR (n=1628 patients)

Creatinine Clearance (need 24-hr urine)

Cockroft-Gault (need weight & BSA)

MDRD

Figure 11 | Performance of the CKD-EPI and MDRD Study equations in estimating measured GFR in the external validation data set. Both panels show the difference between measured and estimated versus estimated GFR. A smoothed regression line is shown with the 95% CI (computed by using the lowest smoothing function in R), using quantile regression, excluding the lowest and highest 2.5% of estimated GFR. To convert GFR from ml/min per 1.73m² to ml/s per m², multiply by 0.0167. CKD-EPD, Chronic Kidney Disease Epidemiology Collaboration; CI, confidence interval; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease. Reprinted with permission from Levey AS, Stevens LA, Schmid CH, et al.87 A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150(9): 604-612.
A Swiss army knife for estimating kidney function: why new equations will not solve the real problem

Wim Van Biesen and Evi V. Nagler

Although patients with elevated serum cystatin C have a higher risk for ESRD, cardiovascular disease, and mortality, this risk may be mediated by factors other than kidney function (ie, GFR). As a result, we do not recommend use of eGFR$_{\text{cystatin C}}$ or eGFR$_{\text{creatinine-cystatin C}}$ to confirm a diagnosis of CKD.
The answer to the question: what are we measuring?
The answer to the question: what are we measuring?

May be:
Why are we measuring?
The Healthy aging kidney
Functional Changes in the Aging Kidney

- Decrease in GFR by 8 ml/min/1.73m²bsa per decade after age 30
- Decrease in renal blood flow
- Increase in glomerular basement membrane permeability
- Decrease in ability to concentrate and dilute urine
- Decrease in ability to excrete acid load
Figure 1. Glomerular filtration rates (by inulin clearance) by age. The solid line represents the mean and the dashed lines represent the standard deviation. Reprinted with permission from Wesson.7
Anatomic and Physiologic Changes in the Aging Kidney

• Glomerulus
  • Glomerulosclerosis
  • Thickening of basement membrane
  • Increase in mesangial matrix

• Tubulointerstitium
  • Tubulointerstitial fibrosis
  • Decrease in tubular number
  • Decrease in tubular length and volume

• Vascular
  • Arteriolsclerosis
  • Hyaline deposition
  • Agglomerulus arteriole
Creatinine, urea, uric acid, water and electrolytes renal handling in the healthy oldest old

- reduced creatinine clearance
- tubular pattern of creatinine back-filtration
- preserved proximal tubule sodium reabsorption and uric acid secretion
- reduced sodium reabsorption in the thick ascending loop of Henle
- reduced free water clearance
- increased urea excretion
- presence of medulla hypotonicity
- reduced urinary dilution and concentration capabilities
- reduced collecting tubules response to furosemide which expresses a reduced potassium excretion in this segment due to a sort of aldosterone resistance
- All physiological changes of the aged kidney are the same in both genders

**Fig. 1.** Factors involved in Cellular Senescence. IGF-1, insulin growth factor-1; TGF, transforming growth factor; TOR, target of rapamycin.
Chronic Inflammation Potentiates Kidney Aging

*Figure 2. Proposed mechanism of oxidative stress–induced MAPK activation and inflammation. ROS from intracellular and extracellular space activates MAP3K such as ASK1 or MEKK1 to phosphorylate MAP2K. The later phosphorylates p38 and JNK, leading to the activation of inflammatory signals. In addition, ROS can decrease the activity of MKP via the oxidation of key cysteine residue in the phosphatase active loop of MKP. Because MKP dephosphorylates MAPK to inactivate MAPK and thus functions as a negative regulator of MAPK, decreased MPK activity leads to either more strongly activated or sustained MAPK signaling, the end result being increased inflammation.*

Figure 2.2 Trends in prevalence of recognized CKD, by race, among Medicare patients aged 65+, 2000-2013

Data Source: Special analyses, Medicare 5 percent sample. Abbreviation: CKD, chronic kidney disease; Af Am, African American; Native Am, Native American.
Figure i.4  Trends in prevalence of recognized CKD, overall and by CKD stage, among Medicare patients aged 65+, 2000-2013

Data Source: Special analyses, Medicare 5 percent sample. Known CKD stages presented as bars; curve showing “All codes” includes known CKD stages (codes 585.1-585.5) and the CKD-stage unspecified codes (585.9, and remaining non-585 CKD codes). Note: In previous years, this graph reported 585.9 codes as a component of the stacked bars.
Abbreviation: CKD, chronic kidney disease. This graphic also appears as Figure 2.1.
An age-calibrated definition of CKD has been proposed to distinguish age-related from disease-related changes in eGFR.

Again, signal versus noise …
Or, are we pathologizing everybody as we age?
Aging v. CKD in the elderly

- Nephrosclerosis in kidney donors: 2 or more of focal and global glomerulosclerosis, tubular atrophy, interstitial fibrosis, and fibrointimal hyperplasia (arteriosclerosis)
- 2.7% in 18-29 year old donors
- 73% in 70-77 year old donors
- The difference in nephrosclerosis comparing two kidneys separated in age by eight years was roughly equivalent to the difference in nephrosclerosis comparing a kidney from a hypertensive donor with a similarly aged nonhypertensive donor

Trajectories of function and biomarkers with age: the CHS All Stars Study

• Gait speed, grip strength, mini-mental status exam, digital symbol substitution test

• IGF-1, DHEAS, IL-6, fibronectin, cystatin-C

• Cystatin-C most consistently associated with decline in all markers

Trajectories of function and biomarkers with age: the CHS All Stars Study

• Gait speed, grip strength, mini-mental status exam, digital symbol substitution test

• IGF-1, DHEAS, IL-6, fibronectin, cystatin-C

• Cystatin-C most consistently associated with decline in all markers

• Caveat for association with advancing renal disease is the presence of other associations

“We live in a world where there is more and more information, and less and less meaning.”

— Jean Baudrillard, Simulacra and Simulation
Counseling patients with CKD due to normal age-related GFR declines — In older adults who are diagnosed with age-related "CKD," a careful explanation is warranted to reassure the patient that a decline in GFR within the range expected for normal aging will have little, if any, effect on his or her life expectancy. Although they may be at higher risk for ESRD because of lower functional reserve (fewer functioning nephrons), this is still a relatively rare event, particularly in the elderly with an eGFR of 45 to 59 mL/min/1.73 m² [108]. Context is particularly relevant, as there are no known therapies that can reverse the age-related decline in GFR. It may also be helpful to discuss that senescence occurs in many other organs such as the skin and the lungs.
Overall, the typical age-related declines in GFR have little, if any, effect on life expectancy, and this point is important in discussions with older adult patients.
The aging kidney that is also failing acutely
MR. FOX, ABOUT YOUR HOMEWORK...

I ASSIGNED QUESTIONS 1 THROUGH 20, YET YOU ONLY DID QUESTIONS 1, 5, 10, 15 AND 20.

I FIGURED YOU COULD PLOT MY RESULTS, FIND THE BEST-FITTING CURVE, AND EXTRAPOLATE HOW I'D DO ON THE OTHERS.

I CAN'T DECIDE IF YOU'RE STUPID OR BRILLIANT, PETER. I COULD SPLIT THE DIFFERENCE AND GIVE ME A "B"...
EPIDEMIOLOGY OF AKI

• INCIDENCE:
  HOSPITAL  5 – 7 %
  COMMUNITY  0.9%

• PRERENAL AKI MOST COMMON ETIOLOGY

• OBSTRUCTIVE UROPATHY IS THE SECOND MOST COMMON CAUSE OF AKI IN THE HOSPITAL

• DRUG NEPHROTOXICITY AND POSTOPERATIVE AKI MOST COMMON IN HOSPITALIZED PATIENTS

• MORTALITY WITH HOSPITALIZED AKI IS 19 – 29 %

• MORTALITY WITH COMMUNITY-ACQUIRED AKI 15 %

• MORTALITY ASSOCIATED WITH AKI INCREASES BASED ON SEVERITY

• AKI IS ASSOCIATED WITH INCREASED RISK FOR NEW ONSET CKD, PROGRESSION OF CKD, ESRD AND MORTALITY.
Increasing Incidence of Community Acquired AKI by Age

Figure 3. Age and incidence of community-acquired AKI. Adapted from Hsu et al.12

Data Source: Special analyses, Medicare 5 percent sample. Age as of January 1 of specified year. All patient-years at risk for Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form, and were alive on January 1 of year shown. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease.
Figure i.13 Unadjusted rates of first hospitalization with AKI for Medicare patients aged 66+, by race and year, 2003-2013

Data Source: Special analyses, Medicare 5 percent sample. All patient-years at risk for Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form, and were alive on January 1 of year shown. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Abbreviations: Af Am, African American; AKI, acute kidney injury; ESRD, end-stage renal disease. This graphic also appears as Figure 5.3.
Figure 5.5 Adjusted hazard of a first AKI hospitalization in Medicare patients aged 66+, overall and dialysis-requiring, by age, 2013

Data Source: Special analyses, Medicare 5 percent sample. Medicare patients aged 66 or older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form, and were alive on 1/1/2013. Dialysis is identified by a diagnosis or charge for dialysis on the AKI inpatient claim or a physician/supplier (Part B) claim for dialysis during the time period of the AKI inpatient claim. Models each include age, race, sex, DM, and CKD status in prior year. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Error bars represent 95% confidence interval of estimates. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease.

Vol 1, CKD, Ch 5 38
<table>
<thead>
<tr>
<th>RIFLE criteria</th>
<th>AKIN criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk</strong></td>
<td></td>
</tr>
<tr>
<td>sCreatinine × 1.5</td>
<td>↑ sCreatinine × 1.5 or ↑ ≥ 0.3 mg/dl in sCreatinine</td>
</tr>
<tr>
<td>Urine output criterion</td>
<td>&lt; 0.5 ml/kg per h × 6 h</td>
</tr>
<tr>
<td><strong>Injury</strong></td>
<td></td>
</tr>
<tr>
<td>sCreatinine × 2</td>
<td>↑ sCreatinine × 2</td>
</tr>
<tr>
<td>Urine output criterion</td>
<td>&lt; 0.5 ml/kg per h × 12 h</td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td></td>
</tr>
<tr>
<td>sCreatinine × 3 or ≥ 0.5 mg/dl if baseline sCreatinine &gt; 4.0 mg/dl</td>
<td>↑ sCreatinine × 3 or ↑ ≥ 0.5 mg/dl if baseline sCreatinine &gt; 4.0 mg/dl</td>
</tr>
<tr>
<td>or anuria × 12 h</td>
<td>or anuria × 12 h</td>
</tr>
<tr>
<td><strong>Loss</strong></td>
<td></td>
</tr>
<tr>
<td>Complete loss of renal function &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>End-stage</strong></td>
<td></td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td></td>
</tr>
</tbody>
</table>

Patients who receive RRT are considered to have met stage 3 criteria, irrespective of the stage they are in at the time of RRT.
Risk factors for acute kidney injury

- Advanced age
- Weight
- Medication
- Chronic kidney disease
- Diabetes mellitus
- Nutritional status
- Hypovolemia
- Sepsis
- Hypertension
- Congestive heart failure
- Hypotension
- Anemia
- Cardiac surgery after a radiocontrast agent

Case #1

• 78 y/o female, PMH lymphedema, HTN, DLD. Meds: furosemide 40 mg/d, atorvastatin 80 mg/d. PCP increased furosemide to 80 mg bid. Patient had syncope, immobilized on floor for 8 hrs before she was found. Treated for AKI, rhabdomyolysis, hypokalemia.

• After hospitalization, transferred to LTC, where she has been maintained on furosemide 40 mg/d, KCl, and atorvastatin 10 mg.
Differential diagnosis of Acute Kidney Injury

- Oliguria
- Azotemia

**PRERENAL**

**RENALE**

**POSTRENEAL**

INCREASED BUN & CREATININE
## Etiology of Prerenal Azotemia & Ischemic AKI

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural lesions</td>
<td>Renal artery stenosis, malignant hypertension, vasculitis</td>
</tr>
<tr>
<td>Volume depletion</td>
<td>Hemorrhage, dehydration, diarrhea, burns</td>
</tr>
<tr>
<td>Reduced effective arterial volume</td>
<td>Decreased cardiac output (CHF, cardiogenic shock, arrhythmia, tamponade) hepatic disease, sepsis, volume redistribution (3rd spacing) from e.g. pancreatitis, peritonitis, crush injuries, burns</td>
</tr>
</tbody>
</table>
ETIOLOGY OF PRERENAL AZOTEMIA & ISCHEMIC AKI

**Drugs**

- NSAID’s
- ACEI’s
- AII antagonists
- vasodilators
- vasoconstrictors
- radiocontrast
- cyclosporine, tacrolimus

**Diuretics**

**Mechanism**

\[ \text{reduction in renal perfusion through alteration in intrarenal hemodynamics} \]

Autoregulation is effective down to a MAP of 80 mmHg in the normal kidney
## NEPHROTOXIC ACUTE KIDNEY INJURY

<table>
<thead>
<tr>
<th>Type of Injury</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agents causing heme-pigment induced toxicity</td>
<td>Cocaine, ethanol, statins</td>
</tr>
<tr>
<td>Agents causing intratubular obstruction</td>
<td>Acyclovir, sulfonamides, ethylene glycol (oxalosis), uric acid, methotrexate</td>
</tr>
<tr>
<td>Acute interstitial nephritis</td>
<td>PCN’s, cephalosporins, sulfonamides, rifampin, quinolones, NSAID’s, thiazides, ppi’s cimetidine, phenytoin, allopurinol, etc., etc., etc.</td>
</tr>
<tr>
<td>Hemolytic-uremic syndrome</td>
<td>CsA, FK506, mitomycin, cocaine, quinine, estrogens</td>
</tr>
</tbody>
</table>
Etiology of drug-induced acute renal injury

• Tubular necrosis: aminoglycosides, amphotericin B, vancomycin, cephaloridine, quinolones, foscarnet
• Interstitial nephritis (immune-mediated): penicillin, methicillin, ampicillin, ciprofloxacin, rifampicin, cephalosporins, clarithromycin, telithromycin, atazanavir, trimethoprim sulfamethoxazole, vancomycin
• Tubular obstruction: acyclovir, sulfanilamide, indinavir, foscarnet, ganciclovir

The aging kidney that is also failing acutely:

POLYPHARMACY
Association between AKI and Duration of Polypharmacy

• Over 20,000 patients hospitalized for AKI in Taiwan in 2006
• Polypharmacy defined as 5+ Rx/day prior to admission
• Variables were age, gender, comorbidities, ICU stay, incident surgeries
• For every duration of polypharmacy >30 days, risk of AKI increased from 10% to 50% (>180 days)
• Odds ratio for AKI at >180 days was 1.74 (p<0.001)
Cumulative Cardiovascular Polypharmacy Is Associated With the Risk of Acute Kidney Injury in Elderly Patients

FIGURE 4. Use of preadmission cardiovascular medications in patients with different severities of acute kidney injury, based on Kidney Disease Improving Global Outcomes criteria. OR=2.58, with increased risk of 30% for every additional CV prescription.

Chao CT, et al. Medicine (Aug 2015); 94(31).

T.S. Dharmarajan MD, MACP, AGSF, a, b, Surya Davuluri MD b

a Massachusetts General Hospital (Wakefield Campus), Harvard Medical School, Boston, MA; b Harvard Medical School, Boston, MA

Table 1

<table>
<thead>
<tr>
<th>Drug Adding Dosage Reduction With Decline in Renal Function (ref 136–138)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihypertensives</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
| | | | **Vitamin 

The list is only a sample of medications that may be used in the nursing home setting.
Biggest Culprits

• Diuretics
• NSAIDs
• ACE/ARBs

• Thus, the biggest culprits are the drugs that affect renal perfusion, i.e., create “intrarenal dehydration”
**DON'Ts in Elderly Psychopharmacology**

- Avoid polypharmacy
- Avoid prescribing to treat side effect of another drug
- Avoid expensive medications while cheapest alternative is available
- Avoid the concept of “a pill for every ill”, i.e., don’t treat every new symptom with another drug
- Avoid therapeutic duplication
- Avoid starting two agents at the same time
- Avoid drugs that are *likely* to cause ADRs in the elderly (e.g., anticholinergics, BZDs)
- Adjust drug dosing based on individual’s renal function
Most important:

Proactive vigilance
Determining the Incidence of Drug-Associated Acute Kidney Injury in Nursing Home Residents

Steven M. Handler MD, PhD, a,b,c,d,e, Pui Wen Cheung MB, f Colleen M. Culley PharmD, c,g Subhasan Perera PhD, h, Sandra L. Kane-Gill PharmD, Mc,d,e,h, John A. Kellum MD, i Zachary A. Marcum PharmD, MS b,c,d

1 Department of Biomedical Informatics, School of Medicine, University of Pittsburgh, Pittsburgh, PA
2 Division of Geriatric Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, PA
3 Geriatric Pharmaceutical Outcomes and Consequences Research and Training Program, University of Pittsburgh, Pittsburgh, PA
4 Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA
5 Department of Medicine, University of Pittsburgh, Pittsburgh, PA
6 Department of Pharmacy and Therapeutics, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA
7 Department of Pharmacy and Therapeutics, School of Pharmacy and Critical Care Medicine, School of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, PA
8 Department of Pharmacy and Therapeutics, School of Pharmacy and Critical Care Medicine, School of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, PA
9 Department of Pharmacy and Therapeutics, School of Pharmacy and Critical Care Medicine, School of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, PA

Table 1

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Medication Class</th>
<th>Medication Class</th>
<th>Medication Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>559 (51.4%)</td>
<td>157 (51.0%)</td>
<td>40 (39.2%)</td>
</tr>
<tr>
<td>ACE(ARBs)</td>
<td>264 (24.4%)</td>
<td>176 (262%)</td>
<td>38 (37.3%)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>193 (18.3%)</td>
<td>59 (20.1%)</td>
<td>38 (37.3%)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>22 (20.4%)</td>
<td>16 (5.6%)</td>
<td>8 (8.2%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>9 (8.1%)</td>
<td>0 (0%)</td>
<td>3 (3.0%)</td>
</tr>
</tbody>
</table>

6172 drug-associated acute kidney injury alerts generated during the 1-year study period.

65 alerts removed for residents on hemodialysis of peritoneal dialysis.

1058 drug-associated acute kidney injury alerts.

2 alerts removed for residents on nonselectively absorbed medications.

1056 drug-associated acute kidney injury alerts.

388 alerts removed for being identical/duplicate alerts.

668 drug-associated acute kidney injury alerts.
The aging kidney that is also failing acutely:

RECOGNIZING VOLUME DEPLETION
## ETIOLOGY OF PRERENAL AZOTEMIA & ISCHEMIC AKI

<table>
<thead>
<tr>
<th><strong>Structural lesions</strong></th>
<th>Renal artery stenosis, malignant hypertension, vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume depletion</strong></td>
<td>Hemorrhage, dehydration, diarrhea, burns</td>
</tr>
<tr>
<td><strong>Reduced effective arterial volume</strong></td>
<td>Decreased cardiac output (CHF, cardiogenic shock, arrhythmia, tamponade) hepatic disease, sepsis, volume redistribution (3rd spacing) from eg. pancreatitis, peritonitis, crush injuries, burns</td>
</tr>
</tbody>
</table>
ETIOLOGY OF PRERENAL AZOTEMIA & ISCHEMIC AKI

Drugs

- NSAID’s
- ACEI’s
- AII antagonists
- vasodilators
- vasoconstrictors
- radiocontrast
- cyclosporine, tacrolimus

Diuretics

Mechanism -----> reduction in renal perfusion through alteration in intrarenal hemodynamics

Autoregulation is effective down to a MAP of 80 mmHg in the normal kidney
Ways the kidney can experience being dry

• **Pathophysiologic**
  - Renal artery stenosis, HF, valvular disease, sepsis, hepatorenal, shock states, hypoalbuminemia

• **Normal physiology**
  - Vomiting, diarrhea, diaphoresis, osmotic diuresis, change in thirst, behavioral change

• **Iatrogenic**, we did it, trying to treat something else
  - Diuretics, NSAIDs, ACD/ARBs, calcineurin inhibitors, other drugs

• **Changes in lifestyle, mobility, access**
  - Reduced mobility, cognitive changes
Case #2

- 91 y/o male, PMH of HTN, AAA, CKD3, D-HF, with dependent edema, on low dose loop blocker tiw.
- Diuretic discontinued
- Patient admitted to hospital for exacerbation of HF, required resumption of diuretic, with stabilization of renal function
Clinical Features of Dehydration

- Dry mucus membranes
- Dry skin, reduced skin turgor
- Reduced axillary sweating
- Orthostatic hypotension
- Tachycardia and hypotension
- Dizziness, headaches
- Cognitive impairment, confusion
- Reduced urine output
- Concentrated urine
- Muscle cramps
- Constipation

Biochemical Features of Dehydration

- Increased BUN and creatinine
- Reduced eGFR
- Increased urea:creatinine ratio
- Hypernatremia
- Increased serum osmolality
- Increased urine osmolality
- Increased urine specific gravity

Is This Elderly Patient Dehydrated? Diagnostic Accuracy of Hydration Assessment Using Physical Signs, Urine, and Saliva Markers

• Prospective diagnostic accuracy study
• 130 patients admitted to hospital for dehydration, mean age 78±9
• Parameters assessed: tachycardia, low systolic BP, dry mucus membranes, dry axilla, poor skin turgor, sunken eyes, capillary refill time, urine color, urine specific gravity, plasma osmolality, BUN:Cr ratio, saliva flow rate, saliva osmolality
• Low SBP was only sign to help in diagnosis
• Saliva osmolality superior to physical signs or urine findings
Management of AKI in the Aging Kidney
Management of AKI in the Aging Kidney

No Silver Bullet
Management of AKI in the Aging Kidney*

- Remove the offending agent(s)
- Support the patient
- Maintain (or restore) hydration

*All I have learned on this subject.
Management of AKI in the Aging Kidney

Be aware of potential complications

• Sepsis
• Anemia
• Platelet dysfunction
• GI bleeding
• Electrolyte abnormalities
• Fluid overload
• CHF, cardiac arrhythmias
• Encephalopathy, etc…
Fig. 1 Stage-based management of acute kidney injury. *Filled boxes* indicate priority actions, which are shown in increasing priority as intensity increases. *Non-filled boxes* indicate actions that are equally appropriate at all stages. This figure was modified from the KDIGO Clinical Practice Guideline. *AKI* acute kidney injury, *ICU* intensive care unit, *KDIGO* Kidney Disease Improving Global Outcomes
MANAGEMENT OF ATN

On the horizon – Maybe some day … or not . . .

• ANP
• Fenoldopam
• NAC
• Growth factors
• Cytokine modulators (role of TNF/NO)
• Adhesion molecule blockade (anti ICAM-1 antibodies)
• Endothelin blockade
• Bioartificial kidney
• Erythropoietin
• Insulin Growth Factor-1
• Alkaline phosphatase
• Intensive Insulin Therapy
• Remote Ischemic Preconditioning
• Sodium Bicarbonate
• Statins
Pendulum of opinion about fluids vs. vasopressors in resuscitation

Fluids = Evil
Pressors = Good

Use both in moderation

Fluids = Good
Pressors = Evil
What are the purposes of IV fluids?

- Maintain intravascular volume
- Maintain overall hydration
- Restore intravascular volume
- Treat hypotension
- Restore overall hydration
- Restore osmolality
- Treat intractable acidosis
- Replace electrolytes
**What is the fluid of choice?**

- Intravascular volume depletion, hypotension: NSS
- Intracellular dehydration: hypotonic fluid, e.g., D5%/0.45NS (but when do you have this in the absence of intravascular depletion?)
- Hypernatremia, hyperosmolality: very hypotonic fluid, D5%/W
- Maintenance hydration: isotonic fluid, e.g., NSS

- How much?
- When to stop diuretics? If, when, how to resume diuretics?
But … recent issues and controversies

• Hypotonic fluid (e.g., D5/½NS) causes hyponatremia, the most common electrolyte abnormality, associated with increased all cause inpatient and 12-month mortality
• BUT, NSS associated with increased normal anion gap metabolic acidosis, may increase ICU morbidity/mortality
• Maybe Ringers Lactate is not such a bad idea, after all …
The expert knows more and more about less and less until he knows everything about nothing.

— Mahatma Gandhi —
Outcomes of AKI in the Aging Kidney
Among hospitalized NH residents, age 85 years or older and several acute conditions, but not chronic conditions, predicted in-hospital mortality. Elderly NH residents at risk of developing these acute conditions may benefit from palliative care.

Outcome of AKI in Relationship to Coincidence or Absence of CKD

Figure 4. Relationship of AKI and CKD to probability of ESRD. Adapted from Ishani et al.30
Hospital Length of Stay in Relationship to Single Acute Organ System Dysfunction

![Bar chart showing median hospital length of stay for different single acute organ system dysfunctions.](chart.png)

*Figure 1. Median hospital length of stay (LOS) stratified by single acute organ system dysfunction (AOSD), including acute renal failure (ARF).*
#### Added Cost Associated With Hospital-Acquired AKI

Table 1. Hospital-Acquired AKI: Mortality and Cost Associated With Selected Changes in Serum Creatinine Level

<table>
<thead>
<tr>
<th>Increase in Serum Creatinine Level</th>
<th>Multivariable OR (95% CI)</th>
<th>Area Under ROC Curve</th>
<th>Increase in Total Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mg/dL</td>
<td>4.1 (3.1-5.5)</td>
<td>0.84</td>
<td>$4,886</td>
</tr>
<tr>
<td>0.5 mg/dL</td>
<td>6.5 (5.0-8.5)</td>
<td>0.86</td>
<td>$7,499</td>
</tr>
<tr>
<td>1.0 mg/dL</td>
<td>9.7 (7.1-13.2)</td>
<td>0.84</td>
<td>$13,200</td>
</tr>
<tr>
<td>2.0 mg/dL</td>
<td>16.4 (10.3-26)</td>
<td>0.83</td>
<td>$22,023</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; ROC, receiving operating characteristic. Adapted from Chertow et al.7
Uncomplicated Acute Renal Failure and Post-Hospital Care: A Not So Uncomplicated Illness

Table 1. Post-hospital care requirements (%) for patients with uncomplicated ARF and other medical conditions following hospital discharge

<table>
<thead>
<tr>
<th>Hospital diagnosis (DRG and ICD-9-CM)</th>
<th>Prevalence¹</th>
<th>Post-hospital care</th>
<th>Extended facility care</th>
<th>Home health care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular disorders except TIA (stroke)</td>
<td>3.2 (n = 16,527)</td>
<td>65</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>Heart failure</td>
<td>7.4 (n = 37,883)</td>
<td>52</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>ARF (uncomplicated)²</td>
<td>0.4 (n = 2,128)</td>
<td>49</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>Pneumonia and pleurisy</td>
<td>8.1 (n = 41,412)</td>
<td>46</td>
<td>29</td>
<td>17</td>
</tr>
<tr>
<td>Circulatory disorders with AMI and complications</td>
<td>2.7 (n = 14,009)</td>
<td>44</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>2.9 (n = 14,790)</td>
<td>37</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>3.6 (n = 18,357)</td>
<td>36</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>Bronchitis and asthma</td>
<td>3.4 (n = 17,182)</td>
<td>14</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

- Factors associated with post-hospital care: age > 65 (increased by decade); female; emergency or outside hospital referral; high severity

Data Source: Special analyses, Medicare 5 percent sample. Medicare patients aged 66 or older who had both Medicare Parts A & B, no Medicare Advantage plan, did not have ESRD on 1/1/2013 and had a first AKI hospitalization in 2013. Institution includes short-term skilled nursing facilities, rehabilitation hospitals, and long-term care facilities. Home also includes patients receiving home health care services. Excludes patients admitted to the acute care hospital from a skilled nursing facility. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease.
Data Source: Special analyses, Medicare 5 percent sample. Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, did not have ESRD, were discharged alive from a first AKI hospitalization in 2011 or 2012, and did not have any claims with a diagnosis of CKD in the 365 days prior to the AKI. Renal status after AKI determined from claims between discharge from AKI hospitalization and 365 days after discharge. Stage determined by S85.x claim closest to 365 days after discharge; ESRD by first service date on Medical Evidence form. Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; ESRD, end-stage renal disease.
Data Source: Special analyses, Medicare 5 percent sample. Medicare patients aged 66 or older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form, and were discharged alive from a first AKI hospitalization in 2011 or 2012. All models censored at the end of Medicare Parts A & B participation, switch to Medicare Advantage program, or 365 days after AKI discharge. Model for ESRD also is censored at death. Model for death is not censored at the start of ESRD. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease.
Figure 5.7  Cumulative probability of a recurrent AKI hospitalization within two years of live discharge from first AKI hospitalization in 2011 for Medicare patients aged 66+, (a) overall, (b) by age, (c) by race, and (d) by chronic kidney disease and diabetes mellitus

(a) Overall

Data Source: Special analyses, Medicare 5 percent sample. Age on January 1, 2011. Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form on 1/1/2011 and were discharged alive from an AKI hospitalization in 2011. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease.
Figure i.14  Cumulative probability of a recurrent AKI hospitalization within two years of live discharge from first AKI hospitalization in 2011 for Medicare patients aged 66+

(b) Age

Data Source: Special analyses, Medicare 5 percent sample. Age on January 1, 2011. Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form on 1/1/2011 and were discharged alive from an AKI hospitalization in 2011. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Abbreviations: AKI, acute kidney injury; ESRD, end-stage renal disease. This graphic also appears as Figure 5.7.

Vol 1, CKD, Intro 86
Figure i.14  Cumulative probability of a recurrent AKI hospitalization within two years of live discharge from first AKI hospitalization in 2011 for Medicare patients aged 66+

(c) Race

Data Source: Special analyses, Medicare 5 percent sample. Age on January 1, 2011. Medicare patients aged 66 and older who had both Medicare Parts A & B, no Medicare Advantage plan, no ESRD by first service date from Medical Evidence form on 1/1/2011 and were discharged alive from an AKI hospitalization in 2011. Censored at death, ESRD, end of Medicare Parts A & B participation, or switch to Medicare Advantage program. Abbreviations: AKI, acute kidney injury; Af Am, African American; ESRD, end-stage renal disease. This graphic also appears as Figure 5.7.
Summary #1

• The normal aging kidney
• The aging kidney that develops CKD
• The aging kidney with AKI
• AKI related to volume depletion
• AKI related to polypharmacy
• Management of AKI
• Outcome of AKI in the aging kidney
Summary #2 – What can I take home?

- Clinical assessment of patients’ fluid status will prevail, for the most part this will beat formulae.
- Ongoing judicious review of patients’ medications—always as few as possible, but just the ones they really need.
- Careful evaluation of ongoing need for diuretics—patients will present difficult balancing acts of multiple variables.
How High is Too High?
<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>Systolic mm Hg (upper #)</th>
<th>Diastolic mm Hg (lower #)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>less than 120</td>
<td>and less than 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 – 139</td>
<td>or 80 – 89</td>
</tr>
<tr>
<td>High Blood Pressure (Hypertension) Stage 1</td>
<td>140 – 159</td>
<td>or 90 – 99</td>
</tr>
<tr>
<td>High Blood Pressure (Hypertension) Stage 2</td>
<td>160 or higher</td>
<td>or 100 or higher</td>
</tr>
<tr>
<td>Hypertensive Crisis (Emergency care needed)</td>
<td>Higher than 180</td>
<td>or Higher than 110</td>
</tr>
</tbody>
</table>
Changes in arterial structure and function that accompany aging.
Hypertension in older persons
Hypertension occurs in more than two-thirds of individuals after age 65. This is also the population with the lowest rates of BP control. Treatment recommendations for older people with hypertension, including those who have isolated systolic hypertension, should follow the same principles outlined for the general care of hypertension. In many individuals, lower initial drug doses may be indicated to avoid symptoms; however, standard doses and multiple drugs are needed in the majority of older people to reach appropriate BP targets.
Recommendation 1
In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥150 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg. (Strong Recommendation – Grade A)

Based on available evidence the panel cannot make a recommendation for a BP goal for people aged 70 years or older with GFR less than 60 mL/min/1.73m². The commonly used estimating equations for GFR were not developed in populations with significant numbers of people older than 70 years and have not been validated in older adults. No outcome trials reviewed by the panel included large numbers of adults older than 70 years with CKD. Further, the diagnostic criteria for CKD do not consider age-related decline in kidney function as reflected in estimated GFR. Thus, when weighing the risks and benefits of a lower BP goal for people aged 70 years or older with estimated GFR less than 60 mL/min/1.73m², antihypertensive treatment should be individualized, taking into consideration factors such as frailty, comorbidities, and albuminuria.
Medications used by elderly patients that can increase blood pressure

• Nonsteroidal anti-inflammatory drugs
  • Aspirin, ibuprofen, naproxen, etc.
• Steroids
  • Prednisone, dexamethasone, methylprednisolone
• Antidepressants
  • Venlafaxine, bupropion, desipramine
• Cough and cold medications
  • Pseudoephedrine, phenylephrine
• Migraine medications
  • Ergotamine, zolmitriptan, sumatriptan
Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis


In this meta-analysis of 123 studies, including >623,000 patients: Blood pressure lowering significantly reduces vascular risk across various baseline blood pressure levels and comorbidities. Our results provide strong support for lowering blood pressure to systolic blood pressures less than 130 mm Hg and providing blood pressure lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease.
Objective: The 2014 Eighth Joint National Committee guidelines for hypertension management emphasize the upper limit of blood pressure (BP) as the target for treatment in the elderly population. Given the uncertainty regarding optimal BP range, we aimed to investigate the association between observed BP and subsequent mortality in older people.

Design, setting, and participants: We extracted data from 128,765 participants 65 years of age who underwent annual health examinations in a retrospective, observational community-based study from 2001 to 2010. Seated BP was measured using an oscillometric device. The outcomes were all-cause and cardiovascular mortality.

Results: As compared to participants with systolic BP at 130 to 139 mm Hg, the risk of all-cause mortality was significantly higher among those with <110 (adjusted hazard ratios [aHRs], 1.12; 95% confidence interval [CI], 1.05-1.20), 140 to 149 (aHR, 1.08; 95% CI, 1.03-1.14), 150 to 159 (aHR, 1.07; 95% CI, 1.01-1.17), 160 to 169 (aHR, 1.11; 95% CI, 1.04-1.19), and 170 mm Hg (aHR, 1.25; 95% CI, 1.17-1.33), whereas the differences were not significant for those with 110 to119 (aHR, 1.06; 95% CI, 1.00-1.12) and 120 to 129 mm Hg (aHR, 1.03; 95% CI, 0.97-1.08). Similarly, diastolic BP at 40 to 79 mm Hg was associated with the lowest risk of all-cause mortality. The J-shaped curve relationship between BP and cardiovascular mortality was also observed.

Conclusions: Observed systolic and diastolic BP other than 110 to 139 and 40 to 79 mm Hg, respectively, were associated with a worse outcome. Our large cohort study supports the J-shaped mortality with observed BP in older people.
Continuous aHRs for all-cause mortality according to SPB (mm Hg) (A) and DBP (B) and for cardiovascular mortality according to SPB (C) and DBP (D). Shi CJ et al. JAMDA 17(2016)654-662

Original Study

Observed Blood Pressure and Mortality Among People Aged 65 Years and Older: A Community-Based Cohort Study

Chia-Jen Shih MD,a,b,c,*, Yung-Tai Chen MD,a,d,*, Shuo-Ming Ou MD,a,c,t, Chi-Hung Lin MD, PhD,c,f, Der-Cheng Tarng MD, PhD,a,c,f,h,*, on behalf of the Taiwan Geriatric Kidney Disease (TGKD) Research Group

JAMDA 17 (2016) 654e662

Fig. 2. Continuous aHRs for all-cause mortality according to SBP (mm Hg) stratified by gender, age, use of antihypertensive medication, DM or CKD status, and established CVD. (A)men, (B) women, (C) age < 80 years, (D) age ≥ 80 years, (E) use of antihypertensive medication (F) without antihypertensive medication, (G) DM and/or CKD, (H) non-DM and non-CKD, (I) CVD, (J) non-CVD. Abbreviations: DM, diabetes mellitus; CKD, chronic kidney disease; CVD, cardiovascular disease.

Fig. 1. Continuous aHRs for all-cause mortality according to SBP (mm Hg) (A) and DBP (mm Hg) (B) and for cardiovascular mortality according to SBP (mm Hg) (C) and DBP (mm Hg) (D).
Blood Pressure: It’s a matter of balance

- Systolic v. diastolic: the dilemma of predominantly systolic hypertension, central arterial stiffening, and widened pulse pressure
- Apparently flexible systolic goal: <150?, <140?, <130? 
- Special conditions, e.g., CKD
- Diastolic pressure, pulse pressure and the J-point revisited
- Increased medication burdens for decreased SBP
- Increased risk of interactions and adverse reactions
“I’m prescribing a patch to help you quit smoking. Wear it over your mouth.”
Thank you!