

Aging Kidney and Fluid Balance

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Disclosures

- Current funding:
 - NIA GEMSSTAR (R03AG050834)
 - Duke CTSA Scholar (UL1TR001117)
 - Duke Claude D. Pepper Older Americans Independence Center (P30 AG028716)
- Other financial relationships: None
- Conflicts of interest: None

Significance

- Aging kidney is not synonymous with chronic kidney disease (CKD)
- CKD is common in adults aged > 65
- Alterations in Kidney Fluid Balance and Urine Production are predominant factors in development of urinary incontinence in older adults



Topic Outline

- Aging Kidney
 - Fluid Balance
 - Urine Production
- CKD
 - Management
 - Complications



NIDDK website

Aging Kidney

- Creatinine Clearance (CrCl) can decline by 0.75ml/min/year in older adults without kidney disease or other comorbidities.
- Not all older adults experience this decline in CrCl.
- Independent of CrCl, kidney physiology changes with aging.

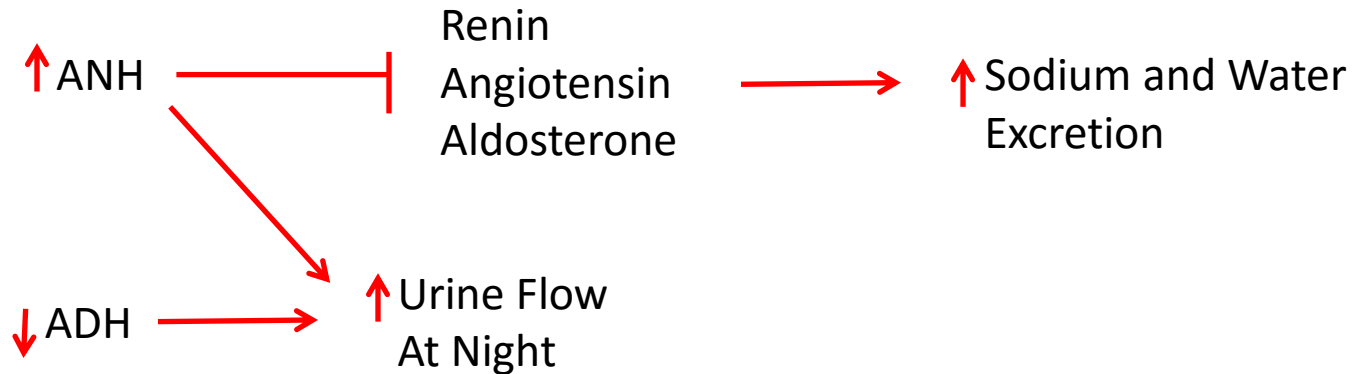
Water and Sodium

- Excess Water loss
 - Maximum urine osmolality declines with age
 - Kidney tubule response to Antidiuretic hormone (ADH) is muted
 - Risk of Dehydration
- “Sodium Wasting”
 - Independent of Volume status
 - Impaired response by Loops of Henle
 - Caused by a decline in Aldosterone levels

Regulation of Urine Formation

Hormone	Effect of Aging on Secretion
Renin-Angiotensin-Aldosterone	Decreased
Atrial Natriuretic Hormone (ANH)	Increased
Antidiuretic Hormone (ADH)	Decreased*

*Decreased Nocturnal Secretion



Nocturnal Urine Production

Circadian Rhythm of ADH secretion typically yields lower urine production at night; however, this changes with older age.

	Young		Old	
	Day	Night	Day	Night
Urine Volume (ml/h)	75	35	50	70
Urine Osmolality (mosm/kg)	700	830	510	450
Plasma AVP (pg/ml)	1.1	2.0	1.9	1.3
Plasma ANH (pg/ml)	19	17	40	55

Nocturnal Polyuria

- 7pm-7am urine volume is more than half of total 24-hr volume.
- Predisposing factors:
 - Aging
 - CKD
 - Edema when recumbent
 - Osmotic diuresis
- Yields increased urinary frequency

Desmopressin Therapy

- AVP analog to reduce urine production, especially at night
 - Effective in small trials
- Evidence seen in Alzheimers disease and other older adults with nocturnal polyuria
- Caution: Older adults with CHF, COPD
- May not be effective in those with CKD

CKD Management

- CKD = GFR $<60\text{ml}/\text{min}/1.73\text{m}^2$ and/or kidney damage

Routine Monitoring involves:

- Hypertension/Volume Overload
- Anemia
- Secondary Hyperparathyroidism
- Metabolic Acidosis

Only **volume status** management has the potential to affect urinary incontinence.

Diuretics

- Small study shows urgency incontinence in CKD patients is associated with high odds of diuretic avoidance
 - OR 5.9, (95% CI 1.5-22.8) (adjusted for age, sex, diuretic type)

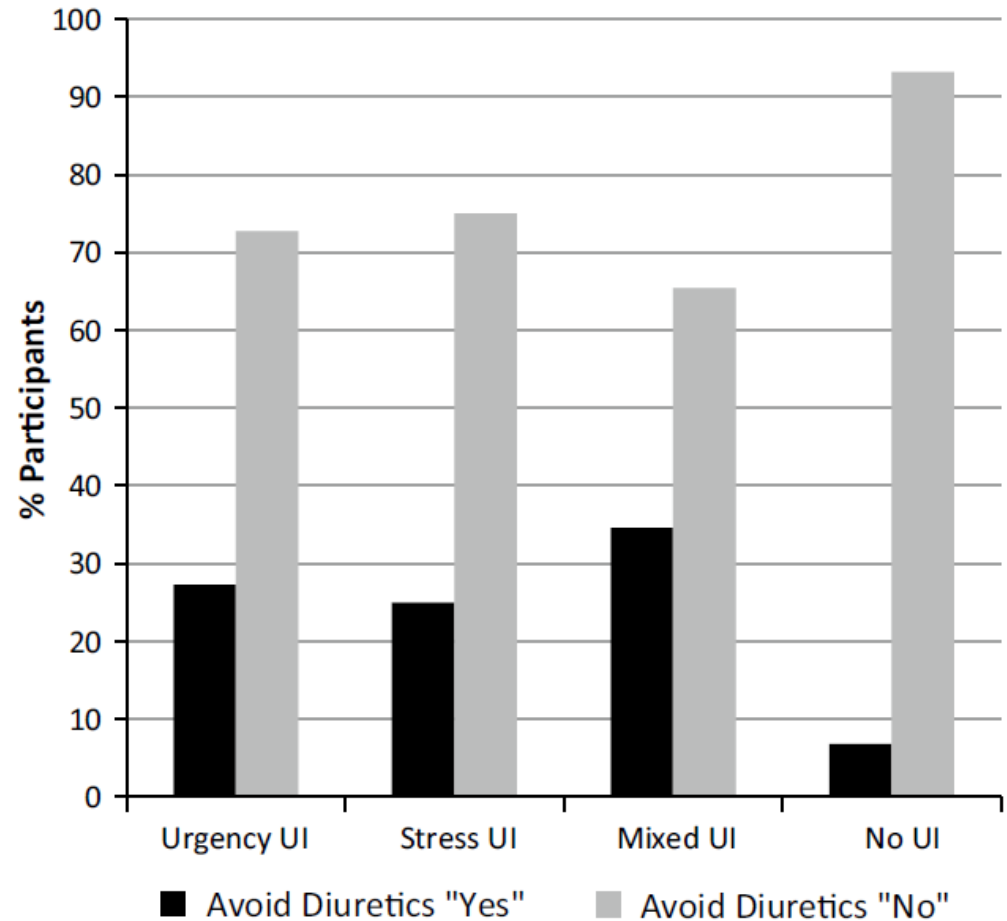


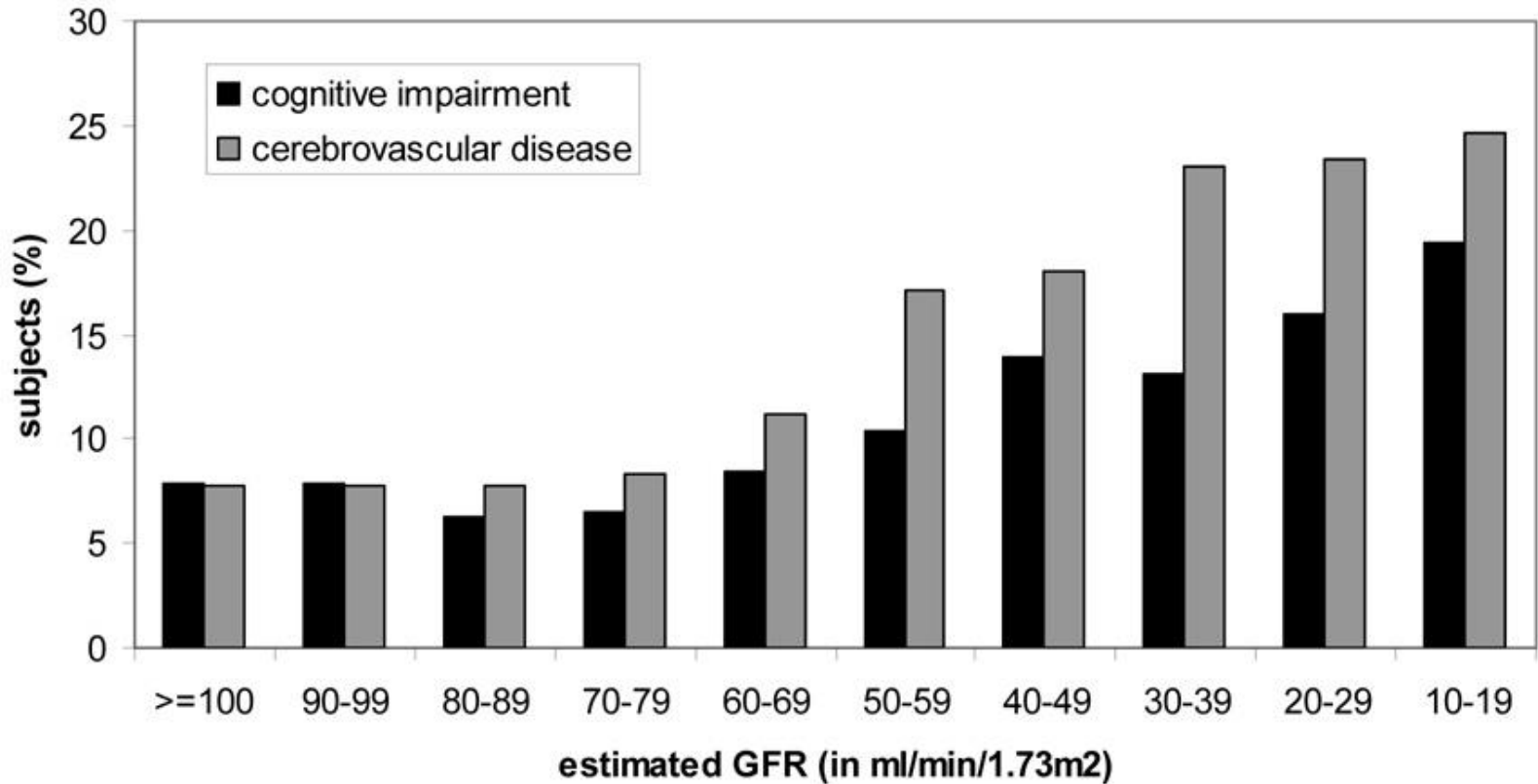
Fig. 1 Self-reported avoidance of diuretics by urinary incontinence type and status
Patel Int Uro Nephrol 2016 PMID27209426

Vitamin D Deficiency

- Secondary hyperparathyroidism can develop in Stage 3 CKD (eGFR <60)
 - 25(OH)D and 1, 25(OH)D fall
 - Proteinuria worsens 25(OH)D deficiency
- 25(OH)D insufficiency (20 to <30 ng/ml) is associated with increased odds for urinary incontinence in community-dwelling older adults.

Vaughn CP Eur J Clin Nutr 2016 PMC5014687

Cognitive Impairment



Kurella-Tamura AJKD 2008 PMC2593146

Albuminuria and low eGFR individually increase risk of Cognitive Impairment.

Kurella-Tamura AJKD 2011 PMC3199339

Knowledge Gaps

Content Area	Knowledge Gap
Fluid Balance	Do some conditions accelerate these aging processes in the kidney? (e.g., acute kidney injury, peripheral vascular disease)
Urine Production	Feasibility of targeted therapy to reverse hormonal changes (e.g., DDAVP) in older adults with CKD
CKD Management	Dose-response of diuretics to UI
CKD Complications	Whether Vitamin D therapy influences UI

Research Opportunities

- Cohort studies in CKD do not typically assess for voiding problems
 - Chronic Renal Insufficiency Cohort (CRIC) Study has an emphasis on older adults (2013-2015)

Ideas for future research approaches:

- Use adherence to diuretics as an outcome in clinical trials
- Use Urinary Incontinence for prognostication of survival in older adults with advanced CKD

Summary

- The kidneys play significant role in the pathophysiology of urinary incontinence.
- The aging kidney and CKD complications should be considered in development of new therapies for urinary incontinence.