Chronic kidney disease and cerebral small vessel disease

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No disclosures
Kidney-brain: Two pulsating organs

- Autoregulation mechanisms
  - Can adapt to blood pressure changes

- Low-resistance
  - Huge network of middle and small size vessels

- High-volume blood flow

- Brain and kidney share features unique to only these two organs
Endothelial dysfunction

Fibrosis and sclerosis

Kang D et al. JASN 2002;13:806-816

Kalimo et al. Future medicine 2008
Quantifying small vessel disease in vivo

- Kidney
  - Reflected in poor clearance
  - Creatinine
  - Cystatin C
  - Microalbuminuria

- Brain
  - White matter lesions
  - Silent infarcts
  - Atrophy
  - Microbleeds
Cerebral small vessel disease

- White matter lesions
- Atrophy
- Silent infarcts
- Microbleeds
Kidney function and cerebral small vessel disease in the Rotterdam Study
Rotterdam Study

- Population-based study
- 490 participants
- eGFR as measure of kidney function
- Brain MRI for automated quantification of small vessel disease
  - White matter lesions
  - White matter atrophy
  - Distinction between lobar and deep regions
Automated quantification
The association between quartiles of kidney function and global brain tissue volumes.

The association between quartiles of kidney function and white matter lesions.

The association between quartiles of kidney function and white matter volumes.

Cardiovascular Health Cognition Study

![Graph showing adjusted prevalence of SBI across gender-specific quintiles of cystatin C.](image)

Gender-specific Quintile of Cystatin C

Test for Linear trend: p<.001

Seliger S L et al. JASN 2005;16:3721-3727
Silent Cerebral White Matter Vascular Risk Factors

Alberto Martinez-Vea, MD, Elena Barbero, MD, Ana Ramos, MD, Carmen Peralta, MD, Montse Broch, PhD, Rosa Pascual-Ahuir, MD, Cristina Gutierrez, PhD, Jose Carlos Marcos, MD, Amadeo Saurí, MD

Prevalence of silent cerebral infarction

HD | Control
---|---
50 | 10

Fig. 1. Comparison of the prevalence of SCI between hemodialysis patients and healthy control group. *p < 0.0001 compared to hemodialysis patients.

Discussion: One third of middle-aged patients seems to be the most important factor that reflects ischemic brain damage caused by generalized vascular damage. *Am J Nephrology*
Patients with chronic kidney disease – with or without hemodialysis have more often cerebral small vessel disease

- White matter lesions
- Silent infarcts

Decreased kidney function in the general population is also associated with cerebral small vessel disease

- White matter lesions
- Silent infarcts
- Atrophy
Cerebral microbleeds

- Hemosiderin deposits
- Visualized using T2* MRI images
- Prevalence in general population is 21%
- Putative risk factor / indicator for stroke and dementia
- Emerging marker of small vessel disease
Cerebral Microbleeds

Cerebral amyloid angiopathy

Arteriosclerotic vasculopathy

Lobar
Deep
Infratentorial
What is known on CKD and microbleeds

- Simple PubMed search using ‘kidney’ and ‘microbleeds’ yields only 10 records…
What we know so far...


- Impaired kidney function is associated with microbleeds in acute stroke patients — Cho et al. Neurology 2009

- Decreased renal function is a risk factor for microbleeds — Chima et al. Nephrol Dial Transplant 2010

- Microalbuminuria is associated with deep and infratentorial microbleeds — Umemura et al. Am J Hypertens 2012
Kidney function and cognition

Barzilay et al. Arch Intern Med 2011
Conclusions

- Kidney small vessel disease shares features with cerebral small vessel disease
- Body of literature linking kidney disease with
  - White matter lesions
  - Silent infarcts
  - Atrophy
- Associations present in clinical series and general population
- Emerging evidence linking kidney disease with microbleeds
- Mechanism of association still unclear
Future perspectives (I) - etiology

- Potential causal pathways:
  - Blood pressure
  - However, multivariable modeling shows independent associations

- Putative causal pathways:
  - Inflammation, homocysteine, nitric oxide

- Common causal factor:
  - Diabetes
  - Blood pressure
  - Genetics
Future perspectives (II) - diagnosis

- Can kidney function be used as predictor for cerebral disease?
- Improvement beyond known risk factors
- Subclinical small vessel disease as endpoint versus clinical disease
- Single measure of kidney function versus combination
Future perspectives (III) - therapy

- Only after causal link has been established

- Preferably, also after improved prediction of persons at increased risk has been established

- Can we reverse the effect of kidney disease on cerebrovascular disease?
Thank you for your attention!