High blood pressure and the kidney: the first victim or the first actor?

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Spain
Kidney causes “primary” hypertension

It is a symptom of renal diseases

It complicates renal failure

“Per se” it causes renal disease
Kidney causes “primary” hypertension
HIGH BLOOD PRESSURE PHYSIOPATOLOGY

KIDNEY

Renal Channels
Nephron Mass

Preload
Ventricular Contraction

Circulating Volumen

Heart Output

BLOOD PRESSURE = HEART OUTPUT x PERIFERAL RESISTANCES

GENETICS

RENIN-ANGIOTENSIN AXIS

Stress

SNS

Insulin

Obesity

Endotelial Factors

Sodium intake

Vessels Tone

Vascular Hypertrophy
HBP AND THE KIDNEY: KEY POINTS

It is a sign of renal disease
Nephritic Syndrome

Inflammation of the glomeruli

HTN

Cola-colored urine (hematuria)

Berger's disease (IgA nephropathy) is the most common cause of primary glomerulonephritis

Oliguria

Peripheral edema

Nephrotic Syndrome

Hypoalbuminemia

Hyperlipidemia

Massive proteinuria

Urine sample
PREVALENCE, AWARENESS, TREATMENT, AND CONTROL OF HYPERTENSION

Table 3  Odds Ratios of Blood Pressure Control Among All Patients with Hypertension

<table>
<thead>
<tr>
<th>Chronic kidney disease stage</th>
<th>Stage 1 (ref)</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stages 4 and 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>1.00</td>
<td>1.18</td>
<td>2.22</td>
<td>2.67</td>
</tr>
<tr>
<td>Stage 2</td>
<td>0.85</td>
<td>1.66</td>
<td>2.98</td>
<td>1.83</td>
</tr>
<tr>
<td>Stage 3</td>
<td>1.64</td>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
<td>3.91</td>
</tr>
<tr>
<td>Stages 4 and 5</td>
<td>.33</td>
<td></td>
<td>&lt;.0001</td>
<td></td>
</tr>
</tbody>
</table>

OR = odds ratio; BMI = body mass index.

AWARENESS, TREATMENT, & CONTROL OF HYPERTENSION

NHANES 1999–2006 participants age 20 & older

USRDS 2010
It complicates renal failure
Prevalence of hypertension, by diagnosis code, race, & year

Table 2.19 (Volume 1)

Medicare patients age 65 & older, surviving all of 2008; ESRD patients excluded.

USRDS 2010
MECANISM OF RENAL LESION: AN OUROBOROS
MECANISMO DE LA LESIÓN RENAL: UN OUROBOROS
PATHOGENESIS OF HBP IN CKD

**HIGH BLOOD PRESSURE**

- **↑RENALASE**
- **↑ENDOTELIN**
- **↑INSULIN RESISTANCE**
- **↑LEPTIN**
- **↑ARTERIAL STIFFNESS**

**INFLAMMATION**

**ADMA**

**ADMA**
Glomerular Hemodynamics

- **Normal Glomerulus**
- **VD afferent arteriole**
  - ↑ Glomerular BP (Hyperfiltration)
- **VC efferent arteriole**
  - ↑ Glomerular BP (Angiotensin II)
INTRAGLOMERULAR BLOOD PRESSURE AND CKD PROGRESSION

Normal

GFR >90 ml/min

Intraglomerular Hypertensión

GFR >135ml/min
Hiperfiltración

CKD STAGE III

GFR <60ml/min

CKD STAGE IV

GFR <30ml/min
GFR reduction > 10% at month 6 were considered as patients with ameliorated hyperfiltration. Those with smaller reductions were categorized as “persistently hyperfiltering.”

From BENEDICT-and DEMAND trials. Iohexol plasma clearance.

Ruggenenti P. Diab Care 2012;35:2061–2068
“Per se” it causes renal disease
ACCELERATED (MALIGNANT) HYPERTENSION

Figure 2. Cumulative proportions of patients with accelerated hypertension surviving at yearly intervals after referral, estimated by the actuarial life-table method.
Multiple Risk Factor Intervention Trial (MRFIT)

Number Screened 361,659 men
Mean Follow-up 15.3 years
Overall incidence of ESRD 17.12/100,000

Result: There was a graded increase in the risk of developing ESRD with higher levels of blood pressure

HIGH BLOOD PRESSURE SEVERITY AND ESRD INCIDENCE: MRFIT

Klag et al. NEJM. 1996
ESRD Due to Any Cause
In 332,544 Men Screened for MRFIT
Adjusted Relative Risk

<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>Adjusted Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>1.0</td>
</tr>
<tr>
<td>Normal</td>
<td>1.2</td>
</tr>
<tr>
<td>High Normal</td>
<td>1.9*</td>
</tr>
<tr>
<td>Stage 1</td>
<td>3.1*</td>
</tr>
<tr>
<td>Stage 2</td>
<td>6*</td>
</tr>
<tr>
<td>Stage 3</td>
<td>11.2*</td>
</tr>
<tr>
<td>Stage 4</td>
<td>22.1*</td>
</tr>
</tbody>
</table>

* p<0.001

§ Men with optimal blood pressure was the reference category.

HTN Linked To Chronic Renal Disease Among 332,544 Men Screened for MRFIT

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www.hypertensiononline.org
BASELINE AGE
MRFIT

ESRD Foreseen

- Normal
- HBP
Prevalence & odds of CKD in NHANES 1999–2006 participants, by method used to estimate GFR, CKD stage, age, gender, race, & severity of disease (%)

<table>
<thead>
<tr>
<th></th>
<th>eGFR MDRD</th>
<th></th>
<th>eGFR CKD-EPI</th>
<th></th>
<th>eGFR cystatin C</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stg 1</td>
<td>Stg 2</td>
<td>Stg 3</td>
<td>Stgs 4-5</td>
<td>Stg 1</td>
<td>Stg 2</td>
</tr>
<tr>
<td>20-39</td>
<td>3.6</td>
<td>1.8</td>
<td>0.5</td>
<td>0.1</td>
<td>ref</td>
<td>4.7</td>
</tr>
<tr>
<td>40-59</td>
<td>3.3</td>
<td>3.9</td>
<td>4.2</td>
<td>0.2</td>
<td>1.6</td>
<td>4.9</td>
</tr>
<tr>
<td>60+</td>
<td>2.3</td>
<td>8.4</td>
<td>26.3</td>
<td>1.8</td>
<td>5.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Male</td>
<td>2.7</td>
<td>4.1</td>
<td>6.0</td>
<td>0.5</td>
<td>ref</td>
<td>3.5</td>
</tr>
<tr>
<td>Female</td>
<td>3.7</td>
<td>4.1</td>
<td>9.4</td>
<td>0.5</td>
<td>1.4</td>
<td>5.0</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>2.2</td>
<td>4.1</td>
<td>9.2</td>
<td>0.5</td>
<td>ref</td>
<td>3.2</td>
</tr>
<tr>
<td>Non-Hispanic Af Am</td>
<td>5.7</td>
<td>4.2</td>
<td>4.8</td>
<td>1.1</td>
<td>1.1</td>
<td>6.3</td>
</tr>
<tr>
<td>Other</td>
<td>6.2</td>
<td>3.9</td>
<td>3.3</td>
<td>0.5</td>
<td>1.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Self-reported diabetes</td>
<td>8.9</td>
<td>12.8</td>
<td>19.4</td>
<td>2.7</td>
<td>2.5</td>
<td>11.8</td>
</tr>
<tr>
<td>Self-reported hypertension</td>
<td>4.1</td>
<td>7.0</td>
<td>16.7</td>
<td>1.6</td>
<td>1.8</td>
<td>5.4</td>
</tr>
<tr>
<td>Self-reported CVD</td>
<td>2.8</td>
<td>8.6</td>
<td>27.9</td>
<td>3.8</td>
<td>2.0</td>
<td>3.3</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4.4</td>
<td>3.7</td>
<td>3.6</td>
<td>0.5</td>
<td>1.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Obese (BMI ≥30)</td>
<td>3.9</td>
<td>5.6</td>
<td>8.0</td>
<td>0.6</td>
<td>1.1</td>
<td>5.5</td>
</tr>
<tr>
<td>All</td>
<td>3.2</td>
<td>4.1</td>
<td>7.8</td>
<td>0.5</td>
<td>ref</td>
<td>4.3</td>
</tr>
</tbody>
</table>


USRDS 2010
Is APOL1 genotype associated with a higher risk of kidney failure?

Methods and cohort
- Retrospective
- Observational study
  - AASK & CRIC cohorts
    - n = 4855

Exposures
- Self-identified race (Black/ non-Black)
- Presence of high-risk APOL1 genotype

Results

<table>
<thead>
<tr>
<th>High-risk APOL1 genotype and risk of kidney failure</th>
<th>1.87</th>
<th>1.22</th>
<th>2.04</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal proteinuria subgroup</td>
<td>1.23 - 2.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High proteinuria subgroup</td>
<td>0.93 - 1.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never developed proteinuria subgroup</td>
<td>1.10 - 3.77</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Black vs non-Black Low risk genotype</th>
<th>0.96</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.85 - 1.10</td>
</tr>
</tbody>
</table>

Conclusion: A high-risk APOL1 genotype is significantly associated with increased kidney failure risk. Screening patients without proteinuria for APOL1 could help providers better identify patients at risk for kidney failure.


Visual Abstract by Denisse Arellano, MD
@denisse.am
RISK OF CHRONIC KIDNEY DISEASE (CKD) DEVELOPMENT ACCORDING BASELINE SERUM CREATININE DISTRIBUTION.

Figure 1. Risk of chronic kidney disease (CKD) development according baseline serum creatinine distribution. 1st quartile (□); SCr: <1 mg/dl for male, <0.7 mg/dl for female. 2nd quartile (○); SCr: 1.0 to 1.1 mg/dl for male, 0.7 to 0.9 mg/dl for female. 3rd quartile (×); SCr: 1.1 to 1.2 mg/dl for male, 0.9 to 1.0 mg/dl for female. 4th quartile (●); SCr: >1.2 mg/dl for male, >1.0 mg/dl for female.
TAKE HOME MESSAGES

• Hypertension is very frequent in CKD, either as cause or consequence.
• Uncontrolled hypertension worsens CKD progression.
• Albuminuria is the better surrogate for renal disease.
• BP control is needed to prevent from ESRD.
THANKS A LOT !
Prevalence of hypertension, by diagnosis code, race, & year

Table 2.19 (Volume 1)

Medicare patients age 65 & older, surviving all of 2008; ESRD patients excluded.
PROGRESS Trial

CV RISK ASSOCIATED TO CKD

- Events
- CV Mortality

CV RISK REDUCTION FOR CKD PATIENTS

- MACE
- STROKE

CKD: 1757 pacientes.
Non CKD: 4148 pacientes.

PREVALENCE OF C.K.D. IN TURKEY

Decreased GFR

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>479</td>
<td>554</td>
</tr>
<tr>
<td></td>
<td>464</td>
<td>416</td>
</tr>
</tbody>
</table>

Increased UAE

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>114</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>2.1</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Postulated tubuloglomerular feedback (TGF) mechanisms in normal physiology, early stages of diabetic nephropathy, and after sodium-glucose cotransporter (SGLT) 2 inhibition.