Arterial Pressure in CKD5 - ESRD Population

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SBP & DBP by Age, Ethnicity & Gender
(US Population ≥ Age 18 Years, NHANES III)

Pulse pressure

Distribution of Hypertension Subtype in the untreated Hypertensive Population in NHANES III by Age

- **ISH (SBP ≥ 140 mm Hg and DBP < 90 mm Hg)**
- **SDH (SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg)**
- **IDH (SBP < 140 mm Hg and DBP ≥ 90 mm Hg)**

Numbers at top of bars represent the overall percentage distribution of untreated hypertension by age.

Difference Between SBP and DBP in CHD Prediction, as a Function of Age*

* Ages 20 to 79
Adjusted for age, sex, & other risk factors

\[ \beta(\text{SBP}) - \beta(\text{DBP}) = 1.49 + 0.029 \times \text{age} \]
\[ (P = 0.008) \]

Franklin et al. *Circulation* 2001;103:1245-1249
Hypertension Control by Age Group

Cross-sectional analysis among 1189 treated hypertensive subjects from Framingham
Lloyd-Jones Hypertension 2000;36:594
Steep Rise in Pulse Pressure With Increasing Age
Data From the Framingham Study


n=2036
Relationship of SBP and DBP to risk for CHD in a dual component model: The Framingham Heart Study

Mean age = 61 years (range: 50-79), n = 1924

Adjusted for age, sex, and other risk factors

P = probability for β coefficients

Cardiovascular Risk Associated with Increasing SBP at Fixed Values of DBP

Two-year risk adjusted for active treatment, sex, age, previous CV complications, and smoking by multiple Cox regression.


EWPHE (n = 840)
SYST-EUR (n = 4695)
SYST-CHINA (n = 2394)
# Blood Pressure and CHD Risk

## Dual BP Component Models

<table>
<thead>
<tr>
<th></th>
<th>Chi Sq.</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>35.6</td>
<td>1.22 (1.15-1.30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP</td>
<td>5.2</td>
<td>0.86 (0.75-0.98)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>0.7</td>
<td>1.04 (0.94-1.16)</td>
<td>NS</td>
</tr>
<tr>
<td>PP</td>
<td>35.6</td>
<td>1.22 (1.15-1.30)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Hazards per 10 mm Hg increment

Adjusted for age, sex, smoking, ECG-LVH, BMI, glucose intolerance, total/HDL cholesterol

Franklin et al. Circulation 1999;100:354
Blood Pressure and Risk for CHD by Age Groups: Results of a Single BP Component† Model

† Adjusted for age, sex, and other risk factors    *P<0.1, **P<0.01, ***P<0.001

Evolution of Systolic and Diastolic BP in CKD patients

Figure 1. Systolic and diastolic BP versus age in the DCI and NHANES populations.
Figure 2. MAP and PP versus age in the DCI and NHANES populations.
### Table 1. Description of Clinical Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>37,069</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>51.3</td>
</tr>
<tr>
<td>Women</td>
<td>48.7</td>
</tr>
<tr>
<td>Age, y</td>
<td>60.1 (15.1)</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>49.9</td>
</tr>
<tr>
<td>Black</td>
<td>43.4</td>
</tr>
<tr>
<td>Asian</td>
<td>1.1</td>
</tr>
<tr>
<td>Native American</td>
<td>0.7</td>
</tr>
<tr>
<td>Other</td>
<td>4.9</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>47.9</td>
</tr>
<tr>
<td>Absent</td>
<td>52.1</td>
</tr>
<tr>
<td>Duration of dialysis prior to study entry, y</td>
<td>3.4 (3.6)</td>
</tr>
<tr>
<td>Laboratory measurements</td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL†</td>
<td>9.6 (3.3)</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.9 (0.4)</td>
</tr>
<tr>
<td>Hematocrit,%</td>
<td>33.3 (3.3)</td>
</tr>
<tr>
<td>Urea reduction ratio, %</td>
<td>68.7 (7.4)</td>
</tr>
<tr>
<td>Predialysis pressure, mm Hg</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>154.3 (20.4)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>79.3 (11.2)</td>
</tr>
<tr>
<td>Pulse</td>
<td>75.0 (15.0)</td>
</tr>
<tr>
<td>Postdialysis pressure, mm Hg</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>139.6 (19.1)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72.7 (10.1)</td>
</tr>
<tr>
<td>Pulse</td>
<td>66.9 (13.9)</td>
</tr>
<tr>
<td></td>
<td>Dippers (n = 24)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 ± 11</td>
</tr>
<tr>
<td>Sex (males/females)</td>
<td>14/10</td>
</tr>
<tr>
<td>Duration of HD (years)</td>
<td>4.2 ± 3.6</td>
</tr>
<tr>
<td>Diabetes [n (%)]</td>
<td>10 (42)</td>
</tr>
<tr>
<td>Hypertentives [n (%)]</td>
<td>12 (50)</td>
</tr>
<tr>
<td>Current smokers [n (%)]</td>
<td>11 (46)</td>
</tr>
<tr>
<td>Duration of follow-up (years)</td>
<td>3.4 ± 1.8</td>
</tr>
<tr>
<td>Ambulatory BP (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Diurnal SBP</td>
<td>160 ± 22</td>
</tr>
<tr>
<td>Diurnal DBP</td>
<td>83 ± 14</td>
</tr>
<tr>
<td>Nocturnal SBP</td>
<td>136 ± 21</td>
</tr>
<tr>
<td>Nocturnal DBP</td>
<td>75 ± 12</td>
</tr>
<tr>
<td>24 h mean SBP</td>
<td>151 ± 19</td>
</tr>
<tr>
<td>24 h mean DBP</td>
<td>81 ± 10</td>
</tr>
<tr>
<td>Predialytic/clinic BP (mmHg)</td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>163 ± 21</td>
</tr>
<tr>
<td>DBP</td>
<td>86 ± 13</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>76 ± 19</td>
</tr>
</tbody>
</table>
One Year Mortality for Patients on Hemodialysis predicted by pulse pressure

Adjusted for level of systolic blood pressure

n = 37,069

Klassen et al. JAMA 2002;287:1548-1555
Brachial Pulse Pressure and Cardiovascular mortality in ESRD patients

Cox model: \( P=0.033 \) adjusted for age and mean BP

Safar ME et al Hypertension 2002
Common Carotid Pulse Pressure and Cardiovascular mortality in ESRD patients

Follow-up (months)

Cardiovascular free events

PPcc <50 mm Hg

PPcc ≤ 75 mm Hg

PPcc ≥ 70 mm Hg

Cox model: $P=0.0049$
adjusted for age and mean BP

Safar ME et al Hypertension 2002
1-year Mortality predicted by SBP
Experience at 782 US dialysis facilities

n = 37,069

Hazard Ratio for Death

Predialysis SBP
Postdialysis SBP

Ref

Categories of SBP (mmHg)

< 115
115 - 125
125 - 135
135 - 145
145 - 155
155 - 165
165 - 175
> 175

Klassen et al. JAMA 2002;287:1548-1555
1-year Mortality predicted by DBP
Experience at 782 US dialysis facilities

Hazard Ratio For Death

DBP (mmHg)

Predicted by DBP

Adjusted for level of systolic blood pressure

Klassen et al. JAMA 2002;287:1548-1555

n = 37,069
Survival curves in hemodialysis patients for each baseline level of diastolic BP

Association between BP and 15-month CV death in 40,933 MHD patients (95% confidence interval bars are depicted). Note that the unadjusted models also include entry quarter. **MICS-adjusted models also include all covariates in the previous models.
All cause mortality according Systolic blood pressure (PAS)

Adjusted Cox  Z-value –2.23; p=0.02
0.992 (0.988-0.991) for 1 mmHg increase

Fouque D et al Observatoire National
All cause mortality according Diastolic blood pressure (PAD)

N = 5692
P < 0.01

Adjusted Cox: Z-value = -6.73; p < 0.001
0.977 (0.971-0.984) for 1 mmHg increase

Fouque D. et al Observatoire National
Mean BP: Cardiac output and peripheral resistance

Systolic pressure: ventricular ejection (stroke volume and ejection time), arterial stiffness, wave reflection

Diastolic pressure: arterial resistance, arterial stiffness, Diastolic decay time
Correlation between arterial pulse pressure, wave reflexion (Augmentation index) aortic pulse wave velocity and stroke volume (n=230)

London et al KI 1996
$\tau$ = R.C
$\alpha$ = $1/\tau$ = $1/R.C$
$\alpha$ = $S/R$

Relationship of Resistance $\bigcirc$, Compliance (C) and Stiffness ($S=1/C$) with diastolic pressure decay

$\tau$-time constant of diastolic decay
$\alpha$-slope of diastolic decay

* log scale

Adapted from Simon et al. Am J Physiol 1979
Interdialysis body weight changes (kg)

Systolic pressure (mm Hg)

Aortic pulse wave velocity-PWV (cm/s)

Stroke volume - SV (mL)

$r = 0.21$

$P = 0.015$

NS-PWV and SV adjusted

$r = 0.284$

$P < 0.01$

Adjust for Systolic BP and PWV

$r = 0.0517$

$P < 0.001$

Adjust for Systolic BP, Age and SV

London et al Kidney Int 1989
Diagrammatic representation of pressure-volume relationships
Correlation between Age and Aortic Pulse Wave Velocity in General population (●) and ESRD patients (●)

- Aortic PWV (m/s) vs. Age (years)
  - General population: $r=0.625$, $p<0.00001$
  - ESRD patients: $r=0.719$, $p<0.00001$

- Characteristic impedance (dynes.s.cm$^{-5}$) vs. Age (years)
  - General population: $r=0.525$, $P<0.00001$
  - ESRD patients: $r=0.340$, $P<0.01$

Age related changes in arterial internal diameters

Controls (r = 0.400; P < 0.01)
ESRD (r = 0.438; P < 0.0001)

Controls (r = 0.525; P < 0.01)
ESRD (r = 0.277; P = 0.065)
Age related changes in Carotid IMTh

Pannier et al. Hypertension 2005
Probability of overall survival in hemodialysis patients according to aortic PWV

Blacher et al. *Circulation.* 1999
All cause survival according to changes in aortic pulse wave velocity (ΔPWV) in response to BP decrease

$\chi^2 = 28.01$

$P < 0.00001$

Changes of mean blood pressure and aortic PWV

<table>
<thead>
<tr>
<th>MBP (mmHg)</th>
<th>PWV (m/s)</th>
<th>MBP (mmHg)</th>
<th>PWV (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion</td>
<td>At target BP</td>
<td>End of follow up</td>
<td>Inclusion</td>
</tr>
<tr>
<td>100</td>
<td>110</td>
<td>120</td>
<td>100</td>
</tr>
</tbody>
</table>

Survivors

Non Survivors

Guérin and al. circulation 2001 ; 103 : 987 - 92
ROC Curve of CV mortality

PWV² = Einc x arterial IMT/arterial radius where Einc is incremental elastic modulus

Schematic representation of reactive hyperemic response in the human forearm after five minutes of ischemia

- Forearm blood flow ml/100 ml/min
- Peak flow
- Flow debt repayment = B/A
- B = Excess hyperemic flow ml/100ml
- Duration of hyperemia

A = Flow debt mL/100 mL
Flow debt repayment (%)

Time to debt repayment (s)

Controls
ESRD

P<0.0001

P<0.0001

Pannier B et al. Kidney Int 2001
Probability of survival in ESRD patients according to postischemic forearm flow debt repayment (FDR)

\[
\chi^2 = 17.9 \\
P < 0.001
\]

FDR > 85%

FDR < 85%

Methods of stimulating increased blood flow

A
Pneumatic cuff
L-NMMA

B
L-NMMA
water bath

C
ACH
L-NMMA

D
ACH

Echotracking is 3 to 10 x more precise than image based techniques

Signal averaging 10-10 000 RF lines

Spatial resolution

<table>
<thead>
<tr>
<th>2 D</th>
<th>TM</th>
</tr>
</thead>
<tbody>
<tr>
<td>200-400 µm</td>
<td>20-40 µm</td>
</tr>
</tbody>
</table>
Graphs show FMD, GTN-induced dilation, and RH in normotensive subjects (white circles and bars) and in patients with essential hypertension (black circles and bars).

Ghiadoni, L. et al. Hypertension 2003;41:1281-1286

Endothelial cell biology and shear stress
### Brachial artery characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Controls</th>
<th>ESRD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline BA diameter (mm)</td>
<td>4.12± 0.13</td>
<td>4.56± 0.11</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BA compliance ($A^2 \cdot kPa \cdot 10^{-7}$)</td>
<td>0.45± 0.02</td>
<td>0.37± 0.02</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BA distensibility ($kPa \cdot 10^{-3}$)</td>
<td>3.5± 0.22</td>
<td>2.6± 0.19</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BA incremental elastic modulus ($kPa \cdot 10^{-3}$)</td>
<td>3.0± 0.22</td>
<td>5.0± 0.42</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BA circumferential wall stress (kPa)</td>
<td>60± 2.5</td>
<td>65± 1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline mean flow velocity (cm/s)</td>
<td>4.6± 0.40</td>
<td>3.4± 0.30</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Baseline mean flow (ml/min)</td>
<td>39± 4.6</td>
<td>33± 3.6</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline mean SR (s$^{-1}$)</td>
<td>53± 2.9</td>
<td>39± 3.5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Baseline peak SR (s$^{-1}$)</td>
<td>365± 23</td>
<td>324± 26</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Whole blood viscosity (cPoise)</td>
<td>3.57± 0.07</td>
<td>2.79± 0.06</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Baseline mean SS (dynes/cm²)</td>
<td>19± 1.15</td>
<td>10.7± 1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Baseline peak SS (dynes/cm²)</td>
<td>129± 9</td>
<td>83± 5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Verbeke et al JASN 2007
Relationship in Controls and ESRD patients between brachial artery (BA) diameter and compliance and BA shear stress

Verbeke et al JASN 2007

Group effect $P<0.01$
Controls

Brachial artery distensibility (kPa10-3)

P < 0.05

TNT-MD (% from baseline)

Verbeke et al. JASN 2007