Echocardiography in Children & Adolescents with Hypertension

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Disclosures:

Elaine M. Urbina, MD, MS

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Outline

• Importance of Echocardiographic measures in assessing CV risk

• Echocardiographic methods:  Structure (LVM), Function (Systolic, Diastolic)

• Abnormalities in cardiac structure and function in youth with high BP
Why? Should Pediatric Providers Care About *High BP in Youth?*

- CVD accounts for 1/3 all cause mortality worldwide & costs billions of dollars and HTN is a major contributor.

*WHO World Health Statistics 2013; Rosamond Circ 2007; figure = Mozaffarian 2016*
What is Proof that HTN Causes TOD in Youth?

- Subjects with coronary plaque had higher antemortem BP.
- Also had thicker renal arteries, the histology seen in adults with HTN.

*P<0.01 for trend, N = 204, 2-39 years; Berenson, NEJM 1998.
How? Do we Assess the Heart in HTN?

- **Structure**
  - LVM, Systolic & Diastolic Function
- **Systolic Function**
  - SF, EF, Strain
- **Diastolic Function**
  - E/A, E/e’, e’a’
LV Mass
Predicts Hard CV Events

• 5,098 participants in the MESA study underwent cardiac MRI at baseline and were followed up for a median of 4 years.
• Subjects with higher LVM relative to volume had a much higher risk of incident CV events including CHD, stroke and Heart Failure.

Bluemke JACC 2008;52:2148.
Systolic Strain Predicts Hard CV Events

- Similarly, subjects with reduced systolic strain, had higher risk for Incident Heart Failure 5.5 years later, independent of CV risk factors.

N=1768; Choi Eur Heart J 2013;34:2354.
Diastolic Function
Predicts Heart Failure with Preserved Ejection Fraction

• Subjects in the Olmsted County Heart Function Study, had diastolic dysfunction measured at baseline and 4 years and had ascertainment for HFpEF at 10 years.
• Not only did the prevalence of diastolic dysfunction increase (24-39%), nearly ¼ of those with diastolic dysfunction saw further deterioration.
• Subjects with progression of diastolic dysfunction (12% of cohort) were more likely to report new onset heart failure even after adjusting for age, HTN, DM and CAD.

N=2042; Kane JAMA 2011;306:856.
• BP-induced thickening of the LV can be measured with standard echocardiography.

• Requirements for High Quality Image
  – Reduce patient movement (sedation)
  – Max resolution (equipment & sonographer dependent)
Echocardiogram: Long Axis View

- RV (Right Ventricle)
- LV (Left Ventricle)
- AO (Aorta)
- LA (Left Atrium)
Echocardiogram: *M*-Mode

\[
0.8 \times (1.04 \times (\text{IVSd} + \text{LVIDd} + \text{PWTd})^3 - \text{LVIDd}^3)) + 0.6 \text{ g}
\]

Devereux et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol. 1986;57:450-8
2-D Measurement of LVM

- Based on mathematical assumptions about ventricular shape.
- Area-Length method or Truncated ellipse.
• M-mode LVM correlated with 2D (r = 0.91), but was consistently higher especially in obese youth.
• Limited normative data using 2-D; US Pediatric cut-points based on M-mode.
Agreement Between Echo & CMR for LV Mass

- Echo overestimated LVM = 190 gm vs 165 gm by CMR (P<.0001) as seen on Bland-Altman plot (mean difference 20 gm).
- Inter-observer error was higher with Echo so that Echo had high sensitivity but low specificity in LVH determination.
- Limited normative values for LVM by CMR, Echo used in Ped HTN guidelines.

N=22 obese youth with HTN; Supe-Markovina J Clin Hypertens 2016;18:976
Indexing LVM
To adjust for differences in body size & age

- Raw LVM or LVM indexed to Ht or BSA do not correct for differences in the size of children (growth is 3-dimensional)
- LVM to $ht^{2.7}$ best eliminates LVM differences across ages but not accurate at youngest ages.
Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents

Experts on the CPG panel evaluated thousands of articles grading the evidence.

Recommendations were then made and also graded.

Published in 2017 in the journal PEDIATRICS.
2017 CPG: Assessment for LVH

• Echo *should be* performed at time of consideration of medication. LVH = LVM >51 g/m$^{2.7}$ if >8* years (*BSA cutpoints also available*)
• ECGs do not provide reliable estimates of LVH so clinicians *should not* perform ECG for evaluation of LVH in youth.
• Repeat echo may be performed to monitor TOD q6-12-mo especially if:
  • Previous echo with LVH or reduced systolic function
  • If persistent stage 1 HTN or higher despite Rx even if first echo normal to assess for development of cardiac injury.
  • Frequent echo not needed in absence of LVH or ↓LV function in subjects with controlled BP.
• The best cut-point to predict hard CV events in adults was an LVMI >51 g/m$^{2.7}$ which predicted a 3.3 times higher risk for an Incident CV event (p < 0.001),

Indexing LVM to height$^{2.7}$ not ideal for children < 9.

- LVMI = 45 g/m$^{2.7}$ Is ~ 97.5$^{th}$ %, the cut-point used to define LVH in adults.

Importance of BP Across the Lifespan

In Predicting Adult LVH

- Adults with LVH had higher long-term BP levels than adults with normal LVM.
- Associations of slopes of systolic BP with adult LVH were significantly positive ($OR = 1.29–1.46; \text{by race/sex } P=0.001–0.008$) in adolescents of 13 to 19 years, adjusting for covariates and were stronger for concentric vs eccentric LVH.
- Adolescence is a crucial period for the development of LVH in later life, which has implications for early prevention.

$N=1154$, Zhang HTN 2018;72:93
• Prevalence of HTN in children of US military members determined from billing data 2006-2011 found 2.6/1000 HTN out of 1.3 million youth aged 2-18.
• Among youth with HTN, 34% (5585) had an echo.
• Overall, 8.0% had LVH or dysfunction. Higher prevalence of LVH in younger subjects may relate to secondary (renal) cause for HTN.

Dobson J Peds 2016;167:92.
Although some obese youth had elevated LVM, the prevalence of LVH was highest in those with both Obesity & HTN.

O/HTN youth had highest LAD & PWV.

Higher LVMI With HTN
Independent of Obesity

- LVMI in O/NT similar to N/weight/HTN.
- Prevalence LVH (38.6 g/m2.7) higher in O/HTN vs O/NT, (51% vs 39%).
- ABPM parameter with strongest correlation with LVMI was mean 24-h SBP

*P<0.004 O/HTN vs O/NT; N=130, Dibeklioglu J Pediatr Endocrinol Metab 2017;30:167
LV Geometry

Relative Wall Thickness*  

- Concentric remodeling
- Concentric hypertrophy
- Normal
- Eccentric hypertrophy

LVMI

- Determine type of pattern using RWT & LVMI
- Concentric hypertrophy:
  - Most common pattern found in HTN
  - Highest risk for adverse CV events

Krumholtz JACC 95

RWT = (IVSd + PWTd) / LVIDd.
LVH was found in 16% of O/HTN youth, and 6% of O/NT.

Most O/HT had Concentric remodeling, not Concentric Hypertrophy.

N=103, mean 14 years; Dusan Pediatr Nephrol 2015;30:645
• Identify at what level of BP does cardiac & vascular target organ damage start to occur in adolescents.
• Determine Ambulatory BP phenotypes predicting CV TOD.
• Investigate how epigenetics influences development of BP-related CV TOD.
Higher LVMI
With Increasing BP

- Recruited from 6 US sites, balanced by BMI.
- LVM index was lower in Low vs. Mid and High BP group.
- Prevalence of LVH by pediatric cut-point: Mid & High 32%.

Mean age 15.5 years; Urbina unpublished data 2019
Concerns With CPG Recommendations

On assessment of LVM

<table>
<thead>
<tr>
<th>SBP%</th>
<th>%False +</th>
<th>%False -</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>29%</td>
<td>9%</td>
</tr>
<tr>
<td>85</td>
<td>23%</td>
<td>12%</td>
</tr>
<tr>
<td>90</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>95</td>
<td>9%</td>
<td>16%</td>
</tr>
</tbody>
</table>

• CPG recommends echo only when considering medication. Therefore, echos are unlikely to be ordered for youth with SBP <95th% or 130/80 which is > than the 90th% of SBP for all girls regardless of height, all boys 13-14 years, and all but tall 15 and 16 year olds.

• 90th% SBP = best balance of false + & false – for predicting LVH suggesting there is little utility in ordering an echo for child with SBP <90th%.

• Reserving echo for youth with SBP > 95th%, will miss 16% of cases of LVH.

P<0.0001 for Logistic Regression model of LVH (LVMI > 38.6 g/m^2.7 = SBP%ile); Urbina unpublished data 2019
Regression of LVMI on wake ambulatory SBP was significant even after adjusting for other ABPM parameters and covariates (including BMI).

\[ R^2 (\text{fully adjusted model}) = 0.38, \ p \leq 0.0001, \ Urbina \ unpublished \ data \ 2019 \]
ABPM Superior in Identifying LVH in Children with HTN

• Odds for LVH higher in youth with HTN diagnosed by ABPM vs. clinic measurement.

*OR does not cross 1; N=160, mean age 12 years; McNiece HTN 2007
Superiority of ABPM & Home BP

In Predicting LVM

- Although Clinic BP was highest (122/71 vs Home 121/69, ABPM 119/67), LVM correlated best with 24-hour SBP from ABPM.
- No significant correlations were found for diastolic BP.

*P<0.01; N=81, mean 13 years; Stergiou Hypertens Res 2011;34:640.
Increase in LVMI Across ABPM Phenotypes

- No significant difference in LVM in WCH vs. NT.
- Increased LVM was found in MH & Sustained HTN.

*p<0.05 vs. normal; Stabouli Ped Neph 2005, N=85, 10-19 yrs
• Although LVMI in WCH was equal to NT, Carotid IMT was elevated in WCH.

*P<0.05 for *different from NT ; †from NT & WCH; N=179, Pall J Hypertens 2010;28:2139.
• WCH more prevalent in Obese youth and Obesity influences LVM, therefore, LVM measured in adolescents matched by age, sex & BMI.
• LVMI in WCH was higher than NT controls.
• LVH was only found in the HTN group (26%).
• WCH may be associated with hypertensive end-organ effects.

• At baseline, 17% of children had LVH (11% eccentric; 6% concentric) & 9% had concentric remodeling. LVH was more common in children with either confirmed (34%) or masked (20%) HTN.
• In multivariable analysis, masked (odds ratio 4.1) and confirmed (odds ratio 4.3) HTN were the strongest independent predictors of LVH.

*P<0.04 difference from NT; †0.1 difference from MH; N=266; Mitsnefes JASN 2010;21:137.
MH Not Benign in Primary HTN

• MH is not benign in primary HTN either.
• Distribution for LVM is skewed towards heavier hearts in MH.

N=592, age 6-18 year; Lurbe HTN 2005;45:493.
• In children referred to HTN clinic, a positive correlation was found between 24-hour weighted BP SD & LVMI ($r=0.389; P=.002$) but no correlation between 24-hour Average Real Variability & LVMI.
• Relationship was lost when adjusted for BMI.

• Non-dipping phenomenon was present in 55% of youth at a HTN clinic (80% renal HTN).
• LVM was higher and prevalence of LVH (LVMI >95th%) was greater in non-dippers (20% vs 9%) but both lost significance after adjustment for age and was not significant in a model including other ABPM parameters.

*P<0.02; N=114, mean 15 years, 70% renal HTN; Seeman Eur J Pediatr 2016;175:1091
Systolic Function of the LV
With “Strain” Calculation

• “Strain” measures the % of myocardial fiber shortening during systole.
• Velocity of fiber shortening can also be measured.
• Reduced (less negative strain) predicts heart failure in adults.

Yip JASE 2003;16:1334-42
• TDI can be performed off-line. Speckle tracking requires special software on the US machine.
• Speckle tracking identifies a speckle (acoustic backscatter generated by reflected US beam) in a designated search region to use as natural acoustic markers that can be tracked from frame to frame. Velocity & strain are obtained by automated measurement of distance between speckles.

• Advantage vs TDI Strain: angle independent, not affected by misalignment between the cardiac axis & US beam.

• Disadvantage: relatively lower frame rates (less resolution); needs specialized software on the echo machine.
Abnormalities in Strain  
In Young Adults Related to BP

- Strain measured with TDI in NT (L=249), Pre-HT (N=25) and HT (N=35) subjects.
- There was a graded decline in systolic function (GLS & GLSr) from NT to Pre-HT to Hypertensive.

* P < 0.0001 for: * N & P < H, †N<P&H; N=309 subjects, mean age 22 years; Urbina unpublished data 2019
Reduced Systolic Strain

With Higher SBP

• Lower (less negative) strain in Mid & High BP groups indicates subtle systolic dysfunction.

N=346, *P ≤ 0.05 L<M& H; Urbina unpublished data 2019
Relationship Between Strain and Diastolic Function with SBP

- Linear relationship between strain and BP.
- DBP remained an independent determinant of strain after adjustment for age, race/ethnicity, adiposity and HR.

\[ R^2 = 0.16 \text{ (fully adjusted model; } p \leq 0.001) \]

Urbina unpublished data 2019
Reduced 3-D Strain
In Adolescents with HTN

• Despite similar EF, youth with HTN had reduced global longitudinal (−15.1 vs −18.5, P<0.0001), & circumferential (−15.2 vs −19.9, P<0.0001), & 3-D strain by speckle tracking (−26.1 vs −31.5, P<0.0001).
• BP remained a significant determinant even after adjusting for BMI & LVM.

N=63, mean 14 HTN, 11 NT; Navrini HTN 2017;70:1142
Diastolic Function:

*Mitral E/A Ratio*

- Doppler effect is change in frequency of wave for observer moving relative to source (when siren approaches, passes, and recedes from an observer the pitch changes).
- Doppler effect used to measure speed & direction of blood flow through Mitral valve.
- The ratio of the heights (E/A velocities) is a measure of diastolic function but it is load (volume) dependent.

Diastolic Function: Tissue Doppler Imaging

- TDI is a less load dependent measure of diastolic function than traditional Doppler.
- Allows quantitative assessment of global & regional function.
- Need special software on echo machine to obtain 2D color-coded TDI images that the software then analyzes.
- Usually performed in the apical 4-chamber view from the LATERAL & SEPTAL aspects of the mitral valve.
• LVH was found in 16.3 % of O/HTN youth, and 5.6 % of O/NT.
• E/A ratio was decreased in both obese groups suggesting obesity as the etiology for the diastolic dysfunction.
• E/A is load dependent.

*P<0.05 differ from Lean; N=103, mean 14 years; Dusan Pediatr Nephrol 2015;30:645

Diastolic Function in Youth with Obesity & Hypertension
• Children (mean 13 years) with untreated HTN confirmed by ABPM had diastolic function compared to controls.

• Despite having higher BMI (HTN=26 vs NT = 23 kg/m²), both groups had normal E/A ratio.

• Only TDI measures differed.

\[ N=46 \text{ case, 34 controls; } *P \leq 0.01; \text{ Agu JASH 2014;8:303.} \]
Diastolic dysfunction (higher E/e’, lower e’/a’) found in HTN youth despite similar age (15 years) and BMI (21 kg/m²).

Among youth with HTN, those with concentric hypertrophy had the worst subclinical systolic and diastolic functions.

*P<0.04 vs normal; N=202; Alp J Am Soc Hypertens 2014;8:303.
Deterioration in Diastolic Function In Young Adults with HTN

- Adolescents examined at baseline (17 years) & after 5 years.
- Diastolic function across multiple measures worsened from N to PreHT to HTN at baseline & follow-up.
- Change in E/e’ was greater at higher levels of BP.

*N=388, 10-23 years; Urbina; unpublished data 2019; *P difference $\leq 0.04$ for $P>N$. 
Diastolic function was lower (E/e’ higher) in the high risk BP group.

*P < 0.003; Urbina unpublished data 2019.
Relationship Between Strain and Diastolic Function with SBP

- There was a linear relationship between SBP and Diastolic Function & BP remained a significant determinant after adjusting for age, race/ethnicity, adiposity and HR.

Decreased Diastolic Function by ABP Phenotype

- E/e’ was higher in MH & HT compared to NT & WC.
- LVMI & PWV higher in WC & HTN.

Urbina unpublished data 2019; P < 0.002 for comparison to: NT & WCH < HT
Increased SBP Load Affects Cardiac TOD

- Daytime SBP load was an independent determinant of all forms of TOD after adjusting for age and sex but lost significance for LVMI after adjusting for BMI%.
- Load percent and load group remained significant determinants of PWV & E/e’ after adjusting for age, sex, BMI% and mean daytime ambulatory SBP (all p < 0.0001).

N=357, mean 15.6 year; *P < 0.0001 Low & Mid < High; Urbina unpublished data 2019.
How Does HTN Hurt the Heart?

Vascular Dysfunction is One Mechanism
• Central BP was a major predictor of Aortic dilation even after adjusting for age and sex.
• LVM was higher in subjects with enlarged Aorta and Aortic size was inversely correlated with Distensibility.
• BP-related arterial stiffness influences LVM.

N=177, Totaro & Urbina J Am Soc Hypertens 2016;10:782
Youth with thicker carotid arteries had less negative strain (poorer systolic function) even after adjusting for other risk factors. Other important determinants were sex, BMI, MAP, HDL & glycemic control.
There is a linear relationship between PWV and measures of cardiac systolic (strain, time to peak strain) and diastolic (e'/a') function which remained significant after adjustment for age, sex, race/ethnicity, adiposity & HR. 

\[ R^2 \text{ (fully adjusted model)} = 0.22 \]

\[ R^2 \text{ (fully adjusted model)} = 0.27 \]

\[ N=357, \text{ mean 15.6 year}; \ *P \leq 0.0001 \text{ Low & Mid < High}; \text{ Urbina unpublished data 2019.} \]
• Plasma Nitric oxide levels were lower in the O/HTN vs O/NT & control groups (p < 0.001).
• NO was negatively correlated with LVMI (p < 0.05) suggesting that endothelial dysfunction impacts cardiac structure.

What Can We Do to Improve the Outcome?

Hippocrates said: “If we could give every individual the right amount of nourishment & exercise, not too little & not too much, we would have found the safest way to health.”

http://www.brainyquote.com/quotes/authors/h/hippocrates.html
First Practice
Primordial Prevention

• Youth with low levels of CV risk factors at baseline (≥3 CVRFs at bottom quartile for BMI, HOMA, BP, TChol/HDL) had lower carotid IMT as an adult.
• cIMT predicts LVM & Systolic strain and CV events.

*All P< 0.013, N=1474, 4-17 years at baseline, 19-41 years at follow-up; Chen Diabetes Care 2005
Next Practice *Primary Prevention: Treating CVRFs Once Identified*

- Obese youth participating in a 12-week weight loss intervention saw a decrease in BMI, **SBP** and **DBP** z-scores over 82 days.

*N=115, Holm 2012 J Hypertens*
Reducing BP

Results in Regression of LVM

• Children with HTN & LVH treated with Enalapril x 15 months saw regression of LVM proportional to SBP reduction.
• Adult studies show regression of LVM with ACEI leads to reduction in CV events.
Improvement in LV Strain with Exercise

• Obese adolescents underwent aerobic exercise for 13 weeks.
• After intervention, Strain improved to near control levels.
• Diastolic function measures also improved.

*P < 0.001; N=10 each group, Ingul Arch Pediatr Adolesc Med 2010
Most adolescents with newly diagnosed HTN had normal geometry but this was less common if HTN was severe.

After 12 months of antihypertensive Rx (lifestyle or with med), prevalence of EH (most common pattern) decreased from 37% to 19% (p = 0.003).

*P<0.003; N=86, mean 14 years; Sladowska-Kozlowski Peiatr Nephrol 2011;26:2201.
**Secondary Prevention: More Aggressive Treatment in High Risk Youth**

- Adolescents treated with lifestyle & medication gained BMI (4%) and had no change in prevalence of elevated BP after 2 years of follow-up.
- Youth treated with Bariatric surgery dropped BMI by 29% & had near total resolution of elevated BP.

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**Graph:**

<table>
<thead>
<tr>
<th></th>
<th>Medical Rx</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% With Elevated BP</strong></td>
<td>Baseline</td>
<td>Follow up</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Follow up</strong></td>
<td>20%</td>
<td>10%</td>
</tr>
</tbody>
</table>

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*Inge Urbina 2018 JAMA Pediatr*
Secondary Prevention

Results in Improvement in Cardiac Structure & Function

- After bariatric surgery extremely obese adolescents with co-morbidities had significant drop in BMI, BP & other CV risk factors.
- Accompanied by a decrease in LVM & improvement in diastolic function.

*P < 0.001; Ippisch JACC 2008, N = 76, 13-20 yrs
Promote Healthy Habits Across the Lifespan to Prevent Hypertensive CV Disease
The ‘Garbage In Garbage Out’ Theory:
We are what we eat!
Find Motivation  To Exercise!
“Consequences of Ignoring the Problem”

Hypertension

Left Ventricular Hypertrophy
Join International Pediatric HTN Association & North American Artery Today!

Welcome to IPHA!

Children can have high blood pressure too! As many as five out of each 100 (5%) children and adolescents may have high blood pressure.

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http://www.iphapediatrichypertension.org

http://naartery.org/

https://naa2019.centerforconferences.uiowa.edu/

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Questions?
Algorithm

BP measurements and classification

Seat child correctly and measure BP by auscultation or by using oscillometric device

Is percentile ≥90th? (Tables 4 and 5)

Yes

Remeasure BP twice and average these 2

Is average ≥90th percentile? (Tables 4 and 5)

No

Normal BP

No

Was repeat auscultatory?

Yes

Remeasure BP twice by using auscultatory technique; average these 2

Is average ≥90th percentile? (Tables 4 and 5)

No

Classify BP according to Table 1

Yes

No
# New definition of BP categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Children (&lt;13 years)</th>
<th>Adolescents (≥13 years)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal BP</td>
<td>&lt;90th % and &lt;120/80</td>
<td>&lt;120/80</td>
</tr>
<tr>
<td>Elevated</td>
<td>≥90th % or ≥120/80 and &lt;95th %</td>
<td>120-129/&lt;80</td>
</tr>
<tr>
<td>Stage 1 HTN</td>
<td>≥95th % and &lt;95th %+ 12 mmHg</td>
<td>130-139/80-89</td>
</tr>
<tr>
<td>Stage 2 HTN</td>
<td>≥95th % + 12 mmHg</td>
<td>≥140/&gt;90</td>
</tr>
</tbody>
</table>

- New BP tables generated excluding youth with obesity shifting the distribution downward for children.
- BP evaluated by % based on sex, age, height in children < 13 years old.
- For adolescents, CPG went to a single cut-point consistent with adult guidelines.

*Same as Adults*
## Cost (not including pro fees)

<table>
<thead>
<tr>
<th>CMR</th>
<th>Echo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CMR = $3240 (no contrast)</strong></td>
<td><strong>2-D limited for LVM = $562</strong></td>
</tr>
<tr>
<td></td>
<td><strong>2-D complete = $1,108 (no Doppler)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>3-D complete = $591</strong></td>
</tr>
</tbody>
</table>
Carotid IMT With Ultrasound

- Most image Carotid, Femoral less reproducible, Aorta possible in younger subjects
- Linear array transducer & Automatic edge detection software
- Use ‘Meijer’s Arc’ for Longitudinal Studies
Increased Carotid IMT With Elevated BP

- Over 700 adolescents & young adults stratified by BP level
- Higher cIMT found in HTN in all segments & pre-HTN had thicker internal cIMT than their normotensive counterparts.

* Urbina, J Clin Htn 2011, P<0.05 for NT<HT, *NT<PreHT&HT.
Pulse Wave Velocity with Tonometry

- Measure distance from Carotid to Femoral Artery with caliper
- Record ECG gated pressure waves at the 2 sites.
Pulse Wave Velocity with Tonometry

- Record ECG gated pressure waves at the 2 sites.
- Device determines pulse transit time to calculate PWV

\[
PWV = \frac{\text{distance}}{\Delta t}
\]

Higher = Stiffer
Higher Arterial Stiffness

With Higher SBP

• Arterial stiffness also increased across BP groups.

P < 0.0001; Urbina unpublished data 2019
Higher PWV with Increasing Ambulatory BP

- SBP remained significant determinant of PWV after adjustments for covariates in a multivariable model.

\[ R^2 \text{ (fully adjusted model)} = 0.31 \quad p = 0.0001, \quad N=303 \]
## Prediction of Daytime Systolic Ambulatory HTN

*Based on Different Clinic SBP%ile Parameters*

<table>
<thead>
<tr>
<th>SBP parameter</th>
<th>AUC</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>80&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>0.829</td>
<td>93.8%</td>
<td>52.5%</td>
</tr>
<tr>
<td>85&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>0.829</td>
<td>87.5%</td>
<td>60.8%</td>
</tr>
<tr>
<td>Elevated SBP</td>
<td>0.672</td>
<td>84.9%</td>
<td>49.4%</td>
</tr>
</tbody>
</table>

- ABPM are not always available and add cost to assessment of BP.
- Logistic regression performed to determine the best clinic SBP%ile to predict daytime ambulatory systolic hypertension.
- The 85<sup>th</sup>%ile performed best.

Hamdani, Urbina, Bekcer Hypertension 2018
Table 3: BP and Echo Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Low (L)</th>
<th>Mid (M)</th>
<th>High (H)</th>
<th>P value</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=144</td>
<td>N=83</td>
<td>N=119</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K1 SBP (mmHg)</td>
<td>111 ± 10</td>
<td>126 ± 6</td>
<td>133 ± 7</td>
<td>&lt;.0001</td>
<td>L&lt;M&lt;H</td>
</tr>
<tr>
<td>K5 DBP (mmHg)</td>
<td>75 ± 10</td>
<td>82 ± 7</td>
<td>86 ± 9</td>
<td>&lt;.0001</td>
<td>L&lt;M&lt;H</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>87 ± 6</td>
<td>97 ± 5</td>
<td>101 ± 7</td>
<td>&lt;.0001</td>
<td>L&lt;M&lt;H</td>
</tr>
<tr>
<td>LVM Index (g/m².7)</td>
<td>31 ± 7</td>
<td>34 ± 7</td>
<td>34 ± 7</td>
<td>0.0009</td>
<td>L&lt;M&amp;H</td>
</tr>
<tr>
<td>E/A ratio (lower worse)</td>
<td>2.36 ± 0.71</td>
<td>2.20 ± 0.64</td>
<td>2.18 ± 0.65</td>
<td>0.085</td>
<td></td>
</tr>
<tr>
<td>E/e' ratio (higher worse)</td>
<td>6.0 ± 1.4</td>
<td>5.8 ± 1.3</td>
<td>6.5 ± 1.5</td>
<td>0.0026</td>
<td>L&amp;M&lt;H</td>
</tr>
<tr>
<td>e'/a' ratio (lower worse)</td>
<td>2.5 ± 0.8</td>
<td>2.3 ± 0.6</td>
<td>2.2 ± 0.6</td>
<td>0.0112</td>
<td>L&gt;H</td>
</tr>
<tr>
<td>Peak Longitudinal Strain (%)</td>
<td>-21.2 ± 3.3</td>
<td>-20.0 ± 3.5</td>
<td>-20.1 ± 3.3</td>
<td>0.0217</td>
<td>L&lt;M&amp;H</td>
</tr>
<tr>
<td>Shortening Fraction (%)</td>
<td>38 ± 4.5</td>
<td>36 ± 5</td>
<td>38 ± 5</td>
<td>0.0536</td>
<td>M&lt;L&amp;H</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>59 ± 7</td>
<td>56 ± 7</td>
<td>56 ± 7</td>
<td>0.0316</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4: General Linear Models

<table>
<thead>
<tr>
<th></th>
<th>E/A log</th>
<th>E/e'</th>
<th>e'/a'</th>
<th>GLS</th>
<th>SF</th>
<th>EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.6</td>
<td>2</td>
<td>2.1</td>
<td>-29.9</td>
<td>38.05</td>
<td>64.26</td>
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<tr>
<td>SBPpct</td>
<td>0.0018</td>
<td></td>
<td></td>
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<tr>
<td>DBPpct</td>
<td>-0.0029</td>
<td>-0.0021</td>
<td>-0.0016</td>
<td>0.037</td>
<td>-0.035</td>
<td>-0.089</td>
</tr>
<tr>
<td>Age</td>
<td>-0.022</td>
<td>-0.019</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td>0.089</td>
<td>-1.35</td>
<td></td>
<td>1.85</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>0.089</td>
<td>-1.35</td>
<td></td>
<td>2.07</td>
<td></td>
</tr>
<tr>
<td>Waist/ht</td>
<td>-0.36</td>
<td>0.4</td>
<td>-0.93</td>
<td>7.74</td>
<td>4.19</td>
<td>-10.21</td>
</tr>
<tr>
<td>HR</td>
<td>-0.0057</td>
<td></td>
<td>-0.0067</td>
<td>0.11</td>
<td>0.14</td>
<td>0.27</td>
</tr>
<tr>
<td>R²</td>
<td>0.14</td>
<td>0.11</td>
<td>0.27</td>
<td>0.16</td>
<td>0.03</td>
<td>0.1</td>
</tr>
</tbody>
</table>

All model p ≤ 0.007 and all parameter estimates p ≤ 0.05
Table 2
Hemodynamics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low Mean</th>
<th>N= 144 SD</th>
<th>Mid Mean</th>
<th>N= 83 SD</th>
<th>High Mean</th>
<th>N= 119 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)**</td>
<td>111.3</td>
<td>9.8</td>
<td>125.8</td>
<td>5.7</td>
<td>132.7</td>
<td>7.4</td>
</tr>
<tr>
<td>SBP percentile (%)**</td>
<td>45.3</td>
<td>25.9</td>
<td>82.8</td>
<td>8.5</td>
<td>94.9</td>
<td>4.1</td>
</tr>
<tr>
<td>DBP (mmHg)**</td>
<td>75.1</td>
<td>10.0</td>
<td>82.1</td>
<td>6.8</td>
<td>85.9</td>
<td>9.2</td>
</tr>
<tr>
<td>MAP (mmHg)**</td>
<td>87.1</td>
<td>9.0</td>
<td>96.6</td>
<td>5.3</td>
<td>101.5</td>
<td>7.1</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>71.7</td>
<td>12.3</td>
<td>69.1</td>
<td>11.8</td>
<td>72.7</td>
<td>12.5</td>
</tr>
<tr>
<td>Pulse Wave Velocity (m/sec)**</td>
<td>4.8</td>
<td>0.7</td>
<td>5.1</td>
<td>0.7</td>
<td>5.4</td>
<td>1.0</td>
</tr>
</tbody>
</table>

P < 0.05 for **L<M<H
PWV is an independent determinant of Cardiac Function

<table>
<thead>
<tr>
<th>General Linear Model*</th>
<th>Time to Peak Strain</th>
<th>e'/'a'</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parameter</strong></td>
<td><strong>β Estimate</strong></td>
<td><strong>β Estimate</strong></td>
</tr>
<tr>
<td>Intercept</td>
<td>2.36</td>
<td>2.24</td>
</tr>
<tr>
<td>PWV</td>
<td>4.78 <strong>(highlighted)</strong></td>
<td>-0.33 <strong>(highlighted)</strong></td>
</tr>
<tr>
<td>Sex</td>
<td>2.02</td>
<td></td>
</tr>
<tr>
<td>Waist/Ht</td>
<td></td>
<td>-0.88</td>
</tr>
<tr>
<td>BMI %</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>0.35</td>
<td>-0.0063</td>
</tr>
<tr>
<td>BMI %*HR</td>
<td>-0.0023</td>
<td></td>
</tr>
<tr>
<td>SBP %</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>R²</td>
<td>0.22</td>
<td>0.27</td>
</tr>
</tbody>
</table>

PWV remained an independent determinant of Time to Peak Strain and Diastolic function after correction for CV risk factors including adiposity and BP.

* All Model p ≤ 0.0001 and all Parameter p ≤ 0.05