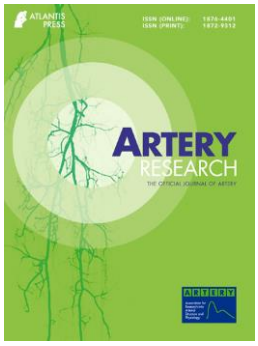

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# 2.7: A HEALTH ECONOMIC EVALUATION ON THE COST EFFECTIVENESS OF HYPERTENSION MANAGEMENT GUIDED BY CENTRAL BLOOD PRESSURE MEASUREMENT: ANALYSIS OF THE BPGUIDE STUDY

S.P. O'Malley, J.E. Sharman

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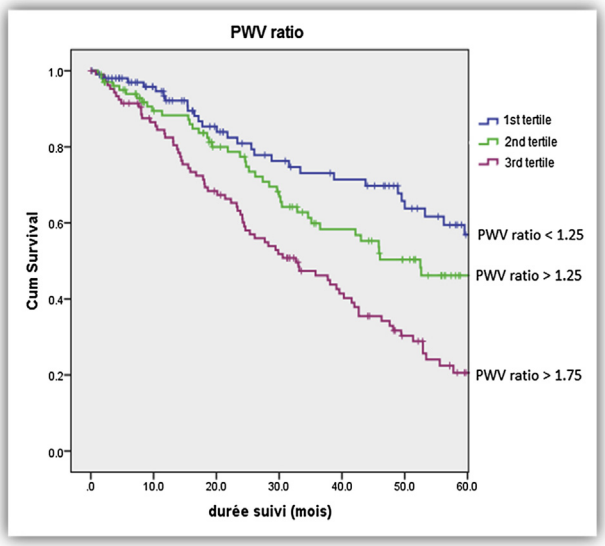
(AVR). Retinal vessel analysis was performed by use of a non-mydriatic vessel analyser (SVA-T) using a computer-based program.
**Results**. Overweight and obese children had higher leptin and insulin levels and reduced adiponectin levels compared to normal weight children ($p < 0.05$). IL-6-levels were significantly higher in obese children compared to normal weight peers ($p < 0.001$). Wider CRVE ($p = 0.031$) and lower AVR ($P = 0.01$) were associated with higher leptin levels. Insulin levels were associated with arteriolar as well as venular dilatation depending on confounder adjustment.
**Conclusions**. All of the above serum risk factors are altered in childhood obesity. However, only leptin and insulin levels are associated with retinal vessel diameter changes, a cumulative microvascular biomarker. Intervention studies are warranted to examine whether lifestyle improvements can prevent alterations of the vasculature early in life.

## 2.5
## AORTIC-BRACHIAL STIFFNESS MISMATCH AND MORTALITY IN DIALYSIS PATIENTS

C. Fortier [2], F. Mac-Way [1,2], S. A. De Serres [1,2], K. Marquis [1], R. Lariviere [1,2], M. S. Utescu [1,2], V. Couture [1,2], M. Agharazii [1,2]
[1]*Chu de Quebec, Quebec City, Canada*
[2]*Université Laval, Quebec City, Canada*

**Objective**. We have shown that regression of brachial stiffness is inversely related to aortic stiffness in dialysis patients. In this study, we sequentially examine the impact of aortic stiffness, brachial stiffness and aortic-brachial stiffness mismatch on mortality in dialysis patients.
**Design and Method**. This is a prospective longitudinal study conducted in 310 adult dialysis patients (mean age 65 ± 15). Aortic and brachial stiffness were respectively measured by determination of carotid-femoral (cf-PWV) and carotid-radial pulse wave velocity (cr-PWV) (CompliorSP-direct measurement technique). Aortic-brachial stiffness mismatch was defined by cf-PWV/cr-PWV mismatch. Central pulse wave profile was determined by radial applanation tonometry. After a mean follow-up of 3.6 ± 1.7 years mortality status was assessed. ROC curve analysis was performed to evaluate the impact of central pulse pressure (PP), heart rate adjusted augmentation index (AIx), cf-PWV, cr-PWV and the cf-PWV/cr-PWV ratio on mortality.
**Results**. The cf-PWV was 13.5 ± 4.1 m/s, cr-PWV was 8.7 ± 1.7 m/s, cf-PWV/cr-PWV ratio was 1.6 ± 0.5, central PP was 49 ± 21 mmHg and the AIx 26.8 ± 11.1%. During follow-up, 160 (49%) deaths occurred. Area under the curve was largest for cf-PWV/cr-PWV ratio (0.694, $p < 0.001$), followed by cf-PWV (0.627, $p < 0.001$), AIx (0.617, $p < 0.001$), PP (0.598 , $P = 0.003$) and cr-PWV (0.371, $p < 0.001$). Figure 1 shows patient survival according to tertiles of aortic-brachial stiffness ratio. In univariate and various adjusted models using Cox regression model, aortic-brachial stiffness was independently associated with increased risk of mortality.
**Conclusion**. Aortic-brachial stiffness mismatch was better that aortic stiffness alone in predicting clinical outcome in this population.




## 2.6
## THE NONLINEAR COMPONENTS OF PULSE PRESSURE: NOVEL MARKERS FOR ARTERIAL STIFFENING WITH PROGNOSTIC SIGNIFICANCE

B. Gavish [1], M. Bursztyn [2]
[1]*Yazmonit Ltd., Eshtaol, Israel*
[2]*Dept. of Internal Med., Hadassah-Hebrew Univ Medical Ctr, Mount-Scopus, Jerusalem, Israel*

Mean ambulatory pulse pressure (PP) is a potent predictor of cardiovascular and all-cause mortality.
**Objectives**. Investigating prognostic significance of elastic and non-elastic PP components
**Methods**. Using a generalized nonlinear pressure—volume relationship in arteries (Fig. 1), PP can be split into an elastic component (PPel) with constant (diastolic) arterial stiffness and a non-elastic component (PPnel) that reflects arterial stiffening during the systole. We determined PPnel, PPel and the ratio WIF=PPnel/PPel ('Widening Factor') from 24-hour ambulatory BP measurements (ABPM) using a model. Standardized hazard ratios (HR) were estimated with Cox proportional hazards regression adjusted to age, gender, body mass index, mean arterial pressure, heart period (HP), systolic- and heart rate-dipping and diabetes and medication status. Assuming an exponential P-V relationship, the model provides the expression WIF=[(K-1)/ln(K)]-1, where K=SD(SBP)/SD(DBP) (SD=standard deviation) and PPel=PP/(1+WIF)
**Results**. ABPM records of 2,105 individuals followed for 5 years for all-cause mortality were analyzed (age 56 ± 16, 55% women, 60% on medication and 9% diabetes, 115 died). Predictive power was demonstrated for patients with slower-than-median pulse rate (HP>0.87 s, $n = 78$): Mean(95%CI) HR of PPnel and WIF were 1.46(1.13-1.90) and 1.64(1.16-2.33) ($P \leq 0.005$), respectively, and 1.59(1.21-2.1) and 1.83(1.27-2.63) ($P = 0.001$) for its subpopulation of older-than-median-age (>58 y, $n = 73$). The corresponding HR for PP was 1.34(1.03-1.75) ($P = 0.03$) and 1.53(1.15-2.03) ($P = 0.004$), respectively. PPel did not display predictive power. Fig. 2 shows that WIF varied strongly with age
**Conclusion**. The 24-hour non-elastic PP component and the Widening Factor, which reflects arterial stiffening during the systole, are novel predictors for mortality, especially in elderly patients with slower pulse.

**Fig.1**

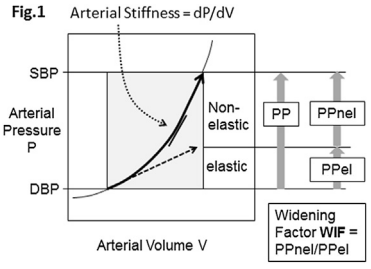
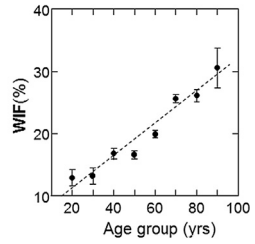



**Fig.2**




## 2.7
## A HEALTH ECONOMIC EVALUATION ON THE COST EFFECTIVENESS OF HYPERTENSION MANAGEMENT GUIDED BY CENTRAL BLOOD PRESSURE MEASUREMENT: ANALYSIS OF THE BPGUIDE STUDY

S. P. O'Malley [1], J. E. Sharman [2]
[1]*Macquarie University, Sydney, Australia*
[2]*University of Tasmania, Hobart, Australia*

**Objectives**. The BPGUIDE study was a prospective, blinded-endpoint study in 286 hypertensive patients randomised to treatment decisions guided by best-practice usual care ($n = 142$) or in addition by central BP measurement ($n = 144$; using SphygmoCor) over twelve months. This study aimed to undertake a health economic assessment to determine cost-effectiveness of hypertension management guided by central BP.
**Methods**. The primary finding of BPGUIDE was that significantly ($p < 0.001$) less antihypertensive medication was used to achieve BP control in patients randomised to central BP guided care.The savings from these reductions in medications were used to determine the cost-effective fee for service and this amount was then compared to the actual financial cost of central BP measurement in order to gauge financial viability.
**Results**. Decreases in 5 antihypertensive medication classes over time were used to calculate financial savings using the Australian Government's Pharmaceutical Benefits Scheme dollar costs. Savings from less use of medications was calculated at $28 to $32/person (each 3 months) using a capital base cost of $10,000 (for the SphygmoCor device), 5 years capital life, 5% discount rate, patient throughput of 50/year and, labour costs up to $250/

hour. Therefore, a fee for service to measure central BP of approximately $30 could be both economically and financially justifiable.
**Conclusions.** Management of hypertension using central BP has cost-savings relating to decreased medication and may be regarded as cost-neutral when factoring in a fee for central BP measurement.

## Oral Session 3

### Young Investigator Oral Presentations

*In association with the European Society of Hypertension Working Group on Vascular Structure and Function*

### 3.1
### OUTCOME-DRIVEN THRESHOLDS FOR AMBULATORY PULSE PRESSURE IN 9938 PEOPLE RECRUITED FROM 11 POPULATIONS

Y.-M. Gu [1], T. Hansen [2], K. Björklund-Bodegård [3], K. Asayama [1,4], Staessen on behalf of the IDACO investigators JA[1,5]
[1]*University of Leuven, Leuven, Belgium*
[2]*Copenhagen University Hospital, Copenhagen, Denmark*
[3]*Uppsala University, Uppsala, Sweden*
[4]*Tohoku University Graduate School of Pharmaceutical Sciences, Sendai, Japan*
[5]*Maastricht University, Maastricht, Netherlands*

**Background.** Evidence-based thresholds for risk stratification based on pulse pressure (PP) are currently unavailable.
**Methods.** To derive outcome-driven thresholds for the 24-h ambulatory PP, we analyzed 9938 people randomly recruited from 11 populations (47.3% women). After age stratification (<60 *vs.* ≥60 years) and using average risk as reference, we computed multivariable-adjusted hazard ratios (HRs) to assess risk by tenths of the PP distribution or risk associated with stepwise increasing (+ 1 mm Hg) PP levels.
**Results.** Among 6028 younger participants (68,853 person-years), the risk of cardiovascular (HR, 1.58; $P = 0.011$) or cardiac (HR, 1.52; $P = 0.056$) events increased only in the top PP tenth (mean, 60.6 mm Hg). Using stepwise increasing PP levels, the lower boundary of the 95% confidence interval of the successive thresholds did not cross unity. Among 3910 older participants (39,923 person-years), risk increased ($p \leq 0.028$) in the top PP tenth (mean, 76.1 mm Hg). HRs were 1.30 and 1.62 for total and cardiovascular mortality, and 1.52, 1.69 for all cardiovascular, cardiac events. The lower boundary of the 95% confidence interval of the HRs associated with stepwise increasing PP levels crossed unity at 64 mm Hg. While accounting for all covariables, the top tenth of PP contributed less than 0.3% (generalized $R^2$ statistic) to the overall risk among elderly.
**Conclusions.** In randomly recruited people, ambulatory PP does not add to risk stratification below age 60; in the elderly, PP is a weak risk factor with levels below 64 mm Hg probably being innocuous.

### 3.2
### LOCAL ARTERIAL STIFFNESS ASSESSED BY ECHO TRACKING IS NOT ASSOCIATED WITH AN INCREASED PULSE WAVE VELOCITY IN HYPERCHOLESTEROLEMIC RABBIT

M. Isabelle, C. Ragonnet, S. Chimenti, C. Badier-Commander, C. Vayssettes-Courchay, N. Villeneuve, J.-P. Vilaine
*SERVIER Research Institute, Suresnes, France*

Arterial stiffness (AS) is generally measured by regional arterial pulse wave velocity (rPWV) or locally by arterial distensibility. Although often used interchangeably, some studies show a weak correlation between these well accepted AS index depending on population. Thus, we aim to investigate in an experimental model of hypercholesterolemic rabbit the comparison between arterial pulse wave velocity and local arterial distensibility. Male New Zealand rabbits (8 week-old) received diet with 0.3% cholesterol for 17 weeks. Under anaesthesia, rPWV was measured with catheters between ascending aorta and illiac artery by the foot-to-foot method. Local arterial stiffness was assessed by echotracking with local PWV using the Moens-Korteweg equation $= (1.050xD)^{-1/2}$, from distensibility as $D = A/AxP$ at different sites: carotid (cPWV), aorta (aPWV and femoral (fPWV). Vessel lesions were analysed by fat red staining.
Table 1 presents the results. As expected, local PWV is comparable in elastic arteries (carotid and aorta) and higher in muscular arteries (femoral artery). Surprisingly, we observe no modification of rPWV and cPWV between the two groups. However, local aPWV and fPWV are increased in hypercholesterolemic rabbits. Only a correlation between the rPWV and local aPWV was observed in control rabbits ($r^2=0.76$ $P = 0.02$). Vessel plaques are more important in aorta and femoral artery than in carotid artery. In conclusion, in a rabbit model of atherosclerosis, we observe an increase in local arterial stiffness in aorta and femoral artery associated with plaques. However, this local stiffening seems to have a weak impact on regional PWV.

**Table 1**

| | rPWV (m/s) | cPWV (m/s) | aPWV (m/s) | fPWV (m/s) |
|---|---|---|---|---|
| Control | 5.0 ± 0.2 | 6.6 ± 0.4 | 5.9 ± 0.2 | 18.8 ± 1.2 |
| Hyperchol | 4.9 ± 0.2 | 6.7 ± 0.4 | 6.9 ± 0.3 * | 25.9 ± 1.8 * |

### 3.3
### TOTAL ARTERIAL ELASTANCE IS MORE STRONGLY ASSOCIATED WITH CARDIOVASCULAR DISEASE THAN CAROTID-FEMORAL PULSE WAVE VELOCITY

C. M. Park, T. Tillin, K. March, N. Chaturvedi, A. D. Hughes
*Imperial College London, London, United Kingdom*

**Background.** Arterial stiffness is associated with an increased risk of cardiovascular disease (CVD) and carotid-femoral pulse wave velocity (cfPWV) is considered as the 'gold standard' measurement method. However cfPWV does not assess the stiffness of the proximal aorta and its sensitivity at higher levels of arterial stiffness, such as in the elderly, has been questioned. We compared associations between CVD and cfPWV and total arterial elastance (TAE) in a cohort of elderly individuals.
**Methods.** 961 individuals (69±6yrs; 76% male) underwent echocardiography (Philips iE33), cerebral MRI, cfPWV (Pulse Trace) and central blood pressure (Pulsecor) measurements. Central pulse pressure and stroke volume were used to calculate TAE. Coronary heart disease (CHD) was defined as a coronary event or revascularisation identified by medical record review, and adjudicated by an independent committee. Cerebrovascular disease was defined as those with infarcts (2+) on MRI or adjudicated history of stroke. Associations are presented as odds ratios (OR) [95% confidence intervals] by logistic regression.
**Results.** A modest correlation was observed between cfPWV and TAE (spearman's rho = 0.14). Associations with CVD were stronger for TAE than cfPWV and subdividing participants based on cfPWV had little effect on associations (Table).

**Table.** Association of cfPWV and TAE with CHD and cerebrovascular disease (adjusted for age, sex and ethnicity). Individuals were also subdivided into two groups based on their cfPWV.

| | All participants $n=961$ | | PWV $< 12$ ms$^{-1}$ $n = 643$ | | PWV $\geq 12$ ms$^{-1}$ $n = 318$ | |
|---|---|---|---|---|---|---|
| | OR [95%CI] | *P* | OR [95%CI] | *P* | OR [95%CI] | *P* |
| **CHD** | | | | | | |
| cfPWV | 1.05 [1.01,1.09] | 0.03 | 1.06 [0.93,1.21] | 0.4 | 1.05 [0.97,1.10] | 0.2 |
| TAE | 2.15 [1.34—3.45] | 0.002 | 2.11 [1.14, 3.91] | 0.02 | 2.00 [0.93,4.30] | 0.07 |
| **Cerebro-vascular disease** | | | | | | |
| cfPWV | 1.04 [0.99,1.08] | 0.1 | 0.99 [0.88,1.12] | 0.9 | 1.01 [0.93,1.10] | 0.8 |
| TAE | 1.40 [0.86-2.26] | 0.2 | 1.54 [0.85,2.80] | 0.2 | 1.12 [0.49,2.59] | 0.8 |