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

B. Gavish, M. Bursztyn

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(AVR). Retinal vessel analysis was performed by use of a non-mydratric 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. Fortier², F. Mac-Way^{1,2}, S. A. De Serres^{1,2}, K. Marquis¹, R. Lariviere^{1,2}, M. S. Utescu^{1,2}, V. Couture^{1,2}, M. Agharazii^{1,2}

¹Chu de Quebec, Quebec City, Canada

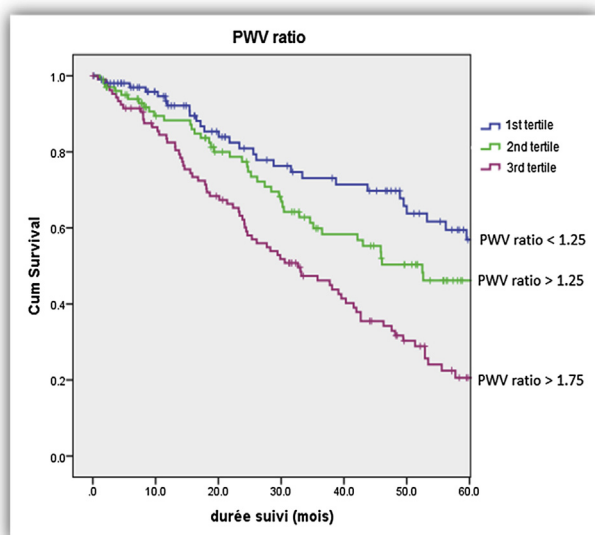
²Université Laval, Quebec City, Canada

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 $26.8 \pm 11.1\%$. 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 than 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. Gavish¹, M. Bursztyn²

¹Yazmonit Ltd., Eshtaol, Israel

²Dept. of Internal Med., Hadassah-Hebrew Univ Medical Ctr, Mount-Scopus, Jerusalem, Israel

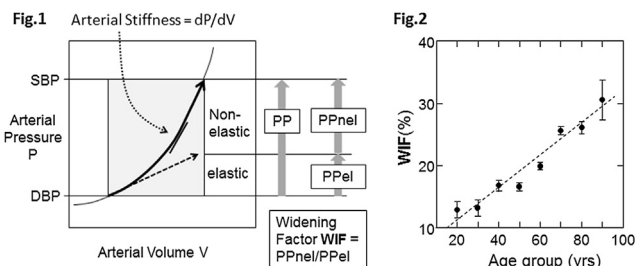
Mean ambulatory pulse pressure (PP) is a potent predictor of cardiovascular and all-cause mortality.

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) ($P < 0.005$), respectively, and 1.59(1.21-2.1) and 1.83(1.27-2.63) ($P = 0.001$) for its sub-population 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.



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'Malley¹, J. E. Sharman²

¹Macquarie University, Sydney, Australia

²University 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/