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3.5: CUFF BLOOD PRESSURE IS PROGRESSIVELY MORE BIASED WITH INCREASING AGE: INDIVIDUAL PARTICIPANT LEVEL ANALYSIS FROM THE INSPECT CONSORTIUM

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conventional risk factors and baseline renal function). These associations remained unchanged after further adjustments for central artery stiffness or traditional central haemodynamic parameters. No other RPA-parameters exhibited significant associations.

Conclusions: These findings demonstrate that baseline INTPR is independently associated with the eGFR reduction in older adults, suggesting that INTPR may play a role in the functional decline of the kidneys.

3.3

ROLE OF ARTERIAL STIFFNESS AND BLOOD PRESSURE VARIABILITY IN THE DEFINITION OF SHATS (SYSTEMIC HEMODYNAMIC ATHEROTHROMBOTIC SYNDROME)

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Background: CV risk exponentially increases as the number of damaged organs increases. The Systemic Hemodynamic Atherosclerotic Syndrome (SHATS) represents a novel conceptualization of the CV continuum focusing on simultaneous multi-organ alteration. This is the first study operationally defining SHATS and aimed at identifying its determinants.

Methods: Left Ventricular Hypertrophy (echocardiography), Common Carotid Artery plaque and increased thickness (ultrasound), and Chronic Kidney Disease (estimated Glomerular Filtration Rate) indexed selective target organ damage. SHATS was operationally defined as their simultaneous presence in a patient. PWV was measured by Sphygmocor[®] and BP variability by 24 h ABPM.

Results: SHATS affected 19.9% of the 367 studied subjects. Subjects with SHATS had a similar prevalence in diabetes mellitus, but a greater prevalence of very stiff artery (84.9 vs 64.3 %, $p < 0.01$) and use of antihypertensive medications. In the presence of similar office BP, SHATS was associated with higher 24 h SBP and lower 24 h DBP (a greater pulsatile pressure!), reduced nighttime SBP fall, and a twofold greater prevalence of reverse dipper status (48.2 vs 20.2 %, $p < 0.001$). BMI (positive correlation) and DBP (negative correlation) were the only traditional CV risk factors significantly associated with the odds of having SHATS. Very stiff artery and BP variability were significant independent determinants of SHATS, with highly predictive accuracy.

Conclusion: SHATS, the simultaneous damage of multiple target organs, may easily operationally defined. Very stiff artery and BP variability represent key factors for SHATS. The present results support the hypothesis of SHATS as a systemic condition, needing further characterization.

3.4

A CLINICAL SCORE TO PREDICT ELEVATED ARTERIAL STIFFNESS: DERIVATION AND VALIDATION IN 3,943 HYPERTENSIVE PATIENTS

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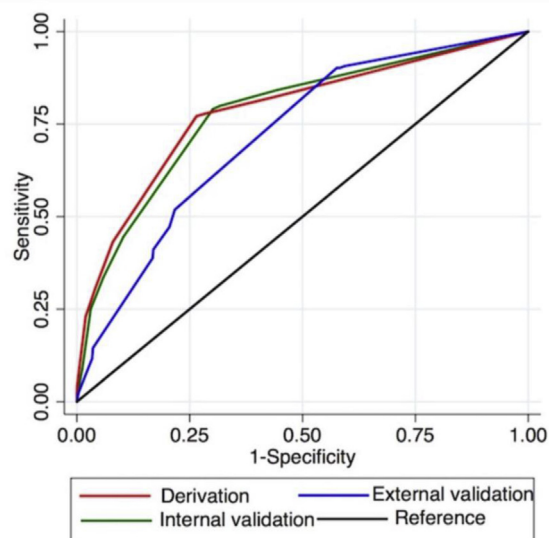
Purpose/Background/Objectives: Aortic stiffness assessed by carotid-femoral pulse wave velocity (PWV) is an important predictor to gauge the overall risk of hypertensive patients; nonetheless, it is underutilized in everyday practice. We derived a simple scoring system based on clinical variables that can identify patients with a priority for measurement of PWV, i.e. those with elevated PWV (≥ 10 m/sec) and at higher risk for events.

Methods: Patient data from three outpatient clinics ($n = 3,943$) were used to form a derivation, internal and external validation cohort. For derivation, independent predictors of high PWV from a binary logistic regression model were dichotomized and implemented in a clinical prediction scoring system with the acronym SAGE (office systolic blood pressure ≥ 160 mmHg: 4 points,

age ≥ 60 years: 4 points, glycemia [blood glucose ≥ 126 mg/dl]: 1 point, eGFR ≤ 60 : 2 points).

Results: Its performance was validated at the internal and external validation cohorts with c-statistics being 0.781 (95% CI: 0.753–0.808) and 0.718 (95% CI: 0.682–0.755) respectively (Figure 1). A cut-off of 5 points to identify patients with high PWV in the external validation cohort yielded a positive predictive value, negative predictive value, sensitivity and specificity of 60.7%, 84.8%, 51.9% and 78.3% respectively.

Conclusions: The SAGE score that takes into account easily measured clinical variables (systolic blood pressure, age, glucose and eGFR) can be used to predict elevated levels of PWV and prioritize its measurement in specific patients. Its use will result in greater acknowledgement of the role of aortic stiffness and aid physicians in implementing it in clinical practice.



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3.5

CUFF BLOOD PRESSURE IS PROGRESSIVELY MORE BIASED WITH INCREASING AGE: INDIVIDUAL PARTICIPANT LEVEL ANALYSIS FROM THE INSPECT CONSORTIUM

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Objectives: Accurate blood pressure (BP) measurement is critical for appropriate hypertension diagnosis and management. Aortic BP represents pressure loading on vital organs and this can be approximated using upper arm cuff BP. With advancing age, cuff systolic BP (SBP) increases and diastolic BP (DBP) decreases (widening pulse pressure [PP]), but whether age may influence cuff BP compared with invasive BP is unknown and was the aim of this study. **Methods:** Cuff BP was measured simultaneously, or near-simultaneously, with invasive aortic BP during catheterization in 1696 individuals within the INSPECT consortium (an international collaboration comprising data from 31 studies and 19 different cuff BP devices [17 oscillometric, 2 mercury sphygmomanometry]). Differences in cuff and invasive BP were assessed using mixed models. **Results:** Subjects were aged 63.3 ± 10.6 years and 32% female. Cuff SBP overestimated invasive aortic SBP in those aged 40–49, but with increasing age there was a progressive increase in the underestimation of aortic SBP (Table). Conversely, cuff DBP systematically overestimated aortic DBP, increasingly with age. Thus, there was a progressively higher error (underestimation) in cuff PP with older age. Adjusting models for sex, mean arterial pressure, heart rate and catheter type did not alter the findings, and no interactions between these parameters and age were found. **Conclusion:** Cuff BP is progressively more biased with increasing age, exposing older people to greater chance for misdiagnosis of risk related to BP. The findings highlight the need to improve cuff BP methods to ensure all people receive appropriate diagnosis and management of hypertension.

Table.

Age category	n	Cuff – invasive systolic BP	Cuff – invasive diastolic BP	Cuff–invasive pulse pressure
40-49 years	170	3.5 [0.5 to 6.6]	4.5 [2.5 to 6.5]	-0.7 [-4.4 to 2.9]
50-59 years	406	0.9 [-1.2 to 2.9]	5.6 [3.7 to 7.4]	-4.6 [-7.2 to -2.1]
60-69 years	558	-0.6 [-3.4 to 2.2]	6.0 [4.1 to 8.0]	-6.7 [-9.6 to -3.9]
70-79 years	456	-3.3 [-5.5 to -1.1]	7.9 [5.6 to 10.2]	-11.0 [-14.2 to -7.9]
80-89 years	106	-4.5 [-8.8 to -0.3]	9.6 [5.9 to 13.2]	-13.8 [-19.2 to -8.5]

Data are mean [95% confidence interval]. BP, blood pressure.

3.6

BLOOD PRESSURE REDUCTION IS THE MAIN DETERMINANT OF THE DE-STIFFENING EFFECT OF ANTIHYPERTENSIVE TREATMENT: A META-REGRESSION ANALYSIS AND COMPARISON WITH ACUTE MODULATION OF TRANSMURAL PRESSURE

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Background: Pulse wave velocity (PWV) is independent predictor of cardiovascular outcomes. Antihypertensive treatment reduces PWV, but it is unknown whether this results from an unloading of stiffer elements in the arterial wall or a structural change in the wall.

Methods: To distinguish between these effects we performed a systematic review and meta-regression analysis of effects of different drug classes and durations of antihypertensive treatment on the relationship between reduction in PWV and that in mean arterial pressure (MAP). We compared this to the variation in PWV during an acute modulation of aortic transmural pressure (TMP) by respiratory manoeuvres, simulating a change in MAP in patients with essential hypertension.

Results: We identified 99 trials on 6,703 hypertensive individuals in total (average age and treatment duration were 56 ± 9.4 years and 21.6 ± 17.9 weeks, respectively). Reduction in PWV was strongly associated with that in MAP, PWV falling by 0.7 m/s per 10 mmHg fall in MAP (95% CI 0.5 – 0.86 m/s, $p < 0.001$). However, reduction in PWV was independent of drug class or duration of treatment. Change in PWV during respiratory manoeuvres was related to TMP with a similar relation to that observed in the meta-regression analysis: 0.94 m/s per 10 mmHg change in TMP (95% CI 0.34 – 1.54 m/s, $p < 0.001$).

Conclusion: Antihypertensive treatment reduces PWV mainly by an unloading effect on the arterial wall, at least over the short term. There is little evidence for a treatment-specific effect. It may be possible to predict effects of antihypertensive treatment on reduction of PWV and pulse pressure by modulating transmural pressure.

3.7

PULSE WAVE VELOCITY IS AN INDEPENDENT RISK FACTOR FOR CARDIOVASCULAR EVENTS, MORTALITY AND DECLINE IN RENAL FUNCTION IN PATIENTS WITH TYPE 1 DIABETES

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Purpose: The prognostic significance of carotid-femoral pulse wave velocity (cfPWV) remains to be determined in patients with type 1 diabetes (T1D). We investigated the predictive value of cfPWV for various endpoints in T1D.

Methods: At baseline, cfPWV was measured using the SphygmoCor device in 652 patients with T1D and various degrees of albuminuria. Endpoints were traced through National Registers and patient records and comprised: composite CVE, mortality, progression in albuminuria, and decline in estimated glomerular filtration rate (eGFR) $\geq 30\%$. Median follow-up ranged from 5.2 to 6.2 years. Slope estimates of eGFR and urinary albumin creatinine rate (UACR) were calculated for a median of 5.5 years. Adjustment included sex, age, mean arterial pressure, LDL cholesterol, smoking, HbA1c, UACR and eGFR at baseline. Hazard ratios (HR) were calculated per 1 standard deviation (SD) increase in cfPWV.

Results: Of the 652 participants (56% male); mean \pm SD age was 54 ± 13 years and cfPWV 10.5 ± 3.38 m/s². After adjustment, higher cfPWV was significantly associated with all endpoints: composite CVE ($n = 81$; HR:1.31; $p = 0.045$); mortality ($n = 48$; HR:1.39; $p = 0.033$); progression in albuminuria ($n = 31$; HR:1.16; $p = 0.012$); and decline in eGFR $\geq 30\%$ ($n = 90$; HR:1.39; $p = 0.015$). Higher cfPWV was associated with a steeper decline in eGFR and a steeper increase in UACR after adjustments ($p \leq 0.009$).

Conclusions: In patients with T1D, higher arterial stiffness was consistently associated with a higher risk of CVE, mortality and decline in renal function, independent of other risk factors. Measurement of cfPWV may have a promising role in risk stratification in T1D.