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4.6: BEAT-BY-BEAT ASSESSMENT OF CARDIAC AFTERLOAD USING AORTIC PU LOOP – A PILOT STUDY

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Our aim was to define the arterial phenotype in mice conditionally inactivated for the integrin α_v subunit in VSMC^{8,9,10} (α_v^{SMKO}) and its role in angiotensin II (AngII)-induced arterial fibrosis. Transgenic mice α_v^{SMKO} and their control littermates (WT) were treated with two doses of AngII, low (0.3 mg/kg/day) and high (1.5 mg/kg/day), for 4 weeks.

At baseline, blood pressure was lower in α_v^{SMKO} compared to WT mice. Carotid distensibility was increased in α_v^{SMKO} mice (13.3 ± 0.7 vs 10.3 ± 0.6 mmHg⁻¹·10⁻³). With low dose AngII isobaric distensibility remained higher in α_v^{SMKO} mice (12.4 ± 1.2 vs 10.7 ± 1.0 mmHg⁻¹·10⁻³). With high dose AngII the increase in collagen content in carotid media was lower in α_v^{SMKO} than in WT (19 vs 35%) for a similar increase in blood pressure (30 mmHg) and arterial wall hypertrophy. Collagen immunostaining and fluorescence measurements (multiphoton microscopy second harmonic generation) confirmed that high dose AngII induced lower increases in collagen content in α_v^{SMKO} mice versus WT (8.9 ± 1.7 vs 14.2 ± 1.4 greyscale mean/pixel). The combination of similar arterial wall hypertrophy with less fibrosis in mutant mice explains an increased distensibility in response to AngII.

The α_v subunit regulates AngII-induced arterial fibrosis as determined by collagen staining, immunostaining and fluorescence. Pharmacological targeting of vascular α_v integrin may have clinical applications in the treatment of patients with fibrosis associated with hypertension and atherosclerosis.

References

- Kappert K, Blaschke F, Meehan WP, Kawano H, Grill M, Fleck E, Hsueh WA, Law RE, Graf K. Integrins alphavbeta3 and alphavbeta5 mediate VSMC migration and are elevated during neointima formation in the rat aorta. *Basic Res Cardiol.* 2001 Feb96(1):42-9.
- Bunni MA, Kramarenko II, Walker L, Raymond JR, Garnovskaya MN. Role of integrins in angiotensin II-induced proliferation of vascular smooth muscle cells. *Am J Physiol Cell Physiol.* 2011 Mar300(3):C647-56.
- Turner CJ, Badu-Nkansah K, Crowley D, van der Flier A, Hynes RO. α_5 and α_v integrins cooperate to regulate vascular smooth muscle and neural crest functions in vivo. *Development.* 2015 Feb 15142(4):797-808.
- Li G, Jin R, Norris RA, Zhang L, Yu S, Wu F, Markwald RR, Nanda A, Conway SJ, Smyth SS, Granger DN. Periostin mediates vascular smooth muscle cell migration through the integrins alphavbeta3 and alphavbeta5 and focal adhesion kinase (FAK) pathway. *Atherosclerosis.* 2010 Feb208(2):358-65.
- Ishigaki T, Imanaka-Yoshida K, Shimojo N, Matsushima S, Taki W, Yoshida T. Tenascin-C enhances crosstalk signaling of integrin $\alpha_v\beta_3$ /PDGFR- β complex by SRC recruitment promoting PDGF-induced proliferation and migration in smooth muscle cells. *J Cell Physiol.* 2011 Oct226(10):2617-24. doi: 10.1002/jcp.22614.
- Michel JB, Li Z, Lacolley P. Smooth muscle cells and vascular diseases. *Cardiovasc Res.* 2012 Jul 1595(2):135-7.
- Galmiche G, Labat C, Mericskay M, Aissa KA, Blanc J, Retailleau K, Bourhim M, Coletti D, Loufrani L, Gao-Li J, Feil R, Challande P, Henrion D, Decaux JF, Regnault V, Lacolley P, Li Z. Inactivation of serum response factor contributes to decrease vascular muscular tone and arterial stiffness in mice. *Circ Res.* 2013 Mar 29112(7):1035-45.
- Hynes RO. Integrins: bidirectional, allosteric signaling machines. *Cell.* 2002 Sep 20110(6):673-87. Review.
- Lacy-Hulbert A, Smith AM, Tissire H, Barry M, Crowley D, Bronson RT, Roes JT, Savill JS, Hynes RO. Ulcerative colitis and autoimmunity induced by loss of myeloid alphav integrins. *Proc Natl Acad Sci U S A.* 2007 Oct 2104(40):15823-8. Epub 2007 Sep 25.
- McCarthy JH, Lacy-Hulbert A, Charest A, Bronson RT, Crowley D, Housman D, Savill J, Roes J, Hynes RO. Selective ablation of alphav integrins in the central nervous system leads to cerebral hemorrhage, seizures, axonal degeneration and premature death. *Development.* 2005 Jan132(1):165-76. Epub 2004 Dec 2.

4.5

U-SHAPED RELATIONSHIP OF RESERVOIR PRESSURE TO CARDIOVASCULAR EVENTS IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

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Objectives: Parameters of aortic stiffness are considered important indicators of cardiovascular risk. However, in heart failure with reduced ejection fraction (HFrEF), their association to outcome was found to be inverted. The aim of this work was to analyze the relationship of the amplitude of reservoir pressure (PresAmp) to cardiovascular events in HFrEF.

Methods: Patients with HFrEF were collected from a cohort undergoing coronary angiography at the hospital Wels-Grieskirchen, Austria. PresAmp was computed from central pressure obtained from radial readings by a generalized transfer function. A combination of myocardial infarction, death, stroke and cardiovascular revascularization served as primary endpoint. Cox-regression analysis and Kaplan-Meier estimates were used for survival analysis.

Results: 83 (9 female) patients were included with a mean age of 61 years. During a median follow-up of 1272 days, 30 patients suffered from the combined endpoint. No significant linear association to outcome was found for PresAmp, brachial or central pulse pressure in Cox-analysis. In all three cases, Kaplan-Meier analysis comparing the respective quartiles indicated a nonlinear, U-shaped relation, but only for PresAmp the increase in risk was significant ($P < 0.05$) in both directions. Although patients with low (16.6 (2.8 SD) mmHg) and high (26.1 (3.2 SD) mmHg) PresAmp showed similar risk, they differed in blood pressure, age, presence of hypertension, presence of coronary artery disease, ventricular dimensions, ejection fraction and diastolic function (table).

Conclusion: We found a U-shaped relation of reservoir pressure to outcome in our population. Pulsatile hemodynamics seem to separate patients with HFrEF into different phenotypes with different prognosis.

Table: Comparison of patients with low (1st quartile) and high (4th quartile) PresAmp. PP, pulse pressure. EF, ejection fraction. LVEDV, left ventricular end-diastolic volume. LVESV, left ventricular end-systolic volume. Values are presented as mean (standard deviation).

Parameter	1 st quartile PresAmp	4 th quartile PresAmp	P-value
N patients	21 (19m/2f)	21 (19m/2f)	
Age, years	57.1 (9.68 SD)	69.4 (9.24 SD)	<0.001
Hypertension	6 (29 %)	19 (90 %)	<0.001
Coronary artery disease	8 (38 %)	14 (67 %)	0.06
Brachial PP, mmHg	31.0 (6.87 SD)	63.0 (8.32 SD)	<0.001
Central PP, mmHg	20.4 (4.08 SD)	48.6 (9.33 SD)	<0.001
E/E ^{medial}	30.8 (15.8 SD)	19.3 (10.0 SD)	0.008
EF, %	22.5 (7.33 SD)	31.6 (7.49 SD)	<0.001
LVEDV, ml	253 (91.3 SD)	162 (64.5 SD)	<0.001
LVESV, ml	199 (75.8 SD)	112 (50.8 SD)	<0.001

4.6

BEAT-BY-BEAT ASSESSMENT OF CARDIAC AFTERLOAD USING AORTIC PU LOOP – A PILOT STUDY

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Purpose/Background/Objectives: Cardiac afterload evaluation is crucial during general anesthesia (GA) especially during hypotension episode. Using beat to beat aortic pressure (P) / flow velocity (U) loop constructed from routine signals recorded during GA might allow to track afterload changes.

Methods: We defined 3 angles characterizing the PU loop (alpha, beta and Global After-Load Angle (GALA) angles). Augmentation index (Aix) and total arterial compliance (Ctot) were also measured via radial tonometry and transfer function. Twenty patients were recruited and classified into low and high cardiovascular (CV) risk group. Vasopressors were administered, when baseline mean arterial pressure (MAP) fell by 20%.

Results: We studied 118 pairs of pre/post bolus measurements. At baseline, patients in the lower CV risk group had higher cardiac output (6.1 ± 1.7 vs

4.2±0.6 L/min meanSD $p < 0.001$), higher Ctot (2.7±1.0 vs 2.0±0.4 ml/mmHg $p < 0.001$), lower Alx (13±10 vs 32±11 % $p < 0.001$) and lower GALA (41±15 vs 68±6 ° $p < 0.001$). GALA was associated with Ctot and Alx. After vasopressors, MAP increase was associated with a decrease in Ctot (2.4±0.9 vs 1.7±0.7 ml/mmHg $p < 0.001$), and an increase in Alx (21±14 vs 25±14 % $p < 0.001$) and GALA (53±18 vs 61±16 ° $p < 0.001$). Changes in GALA and Ctot after vasopressors were strongly associated ($p = 0.004$).

Conclusions: PU Loop assessment from routine hemodynamic optimization management during GA and especially our novel GALA parameter could monitor cardiac afterload continuously in anesthetized patients, and may help clinicians to titrate vasopressor therapy.

4.7

MEASUREMENT OF ARTERIAL STIFFNESS USING A CONNECTED BATHROOM SCALE: CALIBRATION AGAINST SPHYGMOCOR

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Background: Measurement of arterial stiffness (AS) is still considered difficult. We developed a non-invasive technique to assess AS from a connected bathroom scale, based on ballistocardiography (BCG) and impedance plethysmography (IPG).

Methods: We included 198 subjects and patients, 111 for calibration study (cal), 88 for validation study (val), 34% hypertensives, mean age 48±17 years, 50% women. The scale pulse transit time (WS-PTT) was calculated as the difference between BCG systolic signals and IPG blood flow in the foot. Distance was estimated from body height and PWV was calculated. Carotid to femoral transit time (CF-PTT) was measured using Sphygmocor. Spearman and robust multivariate regressions were used.

Results: The WS-PTT correlated well with CF-PTT with $R = 0.69$ in pooled population (cal 0.73, val 0.60). WS-PWV correlated with CF-PWV with $R = 0.73$ (cal 0.67, val 0.59). The standard deviation of difference was 1.19 m/s with no significant bias compared with CF-PWV. Correlations of WS-PWV with age and blood pressure were similar ($R = 0.69$ and 0.60, resp.) to those of CF-PWV ($R = 0.67$ and 0.60, resp.). These good correlations were non-trivial given the differences in wave paths, the fact that measurements are made in orthostatic position and totally investigator-free.

Conclusion: We show in two distinct populations that a simple user-oriented instrument such as a connected bathroom scale can estimate arterial stiffness with accuracy close to healthcare-oriented systems. Because these devices will be used by the general population, the availability of arterial stiffness data on very large, non-medicalized populations will change our management of well-being and health.

4.8

INCREASED CARDIAC WORKLOAD IN THE UPRIGHT POSTURE IN MALE SUBJECTS: NON-INVASIVE HEMODYNAMICS IN MEN VERSUS WOMEN

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Background: Men and women differ in the risk of cardiovascular disease, but the underlying mechanisms are not completely understood. We examined possible sex-related differences in supine and upright cardiovascular regulation.

Methods: Hemodynamics were recorded from 167 men and 167 women of matching age (~45 years) and body mass index (~26.5 kg/m²) during passive head-up tilt. None had diabetes, cardiovascular disease other than hypertension, or antihypertensive medication. Whole-body impedance cardiography, tonometric radial blood pressure, and heart rate variability were analyzed. Results were adjusted for height, smoking, alcohol intake, mean arterial pressure, plasma lipids and glucose.

Results: Supine hemodynamic differences were minor: lower heart rate (-4%) and higher stroke volume (+7.5%) in men than women ($p < 0.05$ for both). Upright systemic vascular resistance was lower (-10%), but stroke volume (+15%),

cardiac output (+16%), and left cardiac work were clearly higher (+20%) in men than women ($p < 0.001$ for all). Corresponding results were observed in a subgroup of men and postmenopausal women ($n = 76$, age >55 years). Heart rate variability analyses showed higher low frequency to high frequency ratio in supine ($p < 0.001$) and upright ($p = 0.003$) positions in men.

Conclusions: The foremost difference in cardiovascular regulation between sexes was higher upright hemodynamic workload of the heart in men, a finding not explained by known cardiovascular risk factors or hormonal differences before menopause. Heart rate variability analyses indicated higher sympathovagal balance in men regardless of body position. The deviations in upright hemodynamics could play a role in the differences of cardiovascular risk between men and women.

4.9

PROPORTIONAL PRESSURE RELATIONS IN THE PULMONARY ARTERIAL SYSTEM

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Background – Objectives: The pulmonary arterial system can be characterized by:

1. A constant product of Pulmonary Vascular Resistance (PVR) and Total Arterial Compliance (TAC) with $\text{Tau} = \text{PVR} \times \text{TAC} \approx 0.7$ seconds (1).

2. A proportional relation exists between systolic and diastolic pulmonary artery pressure, sPAP, dPAP, with mean pulmonary artery pressure mPAP (2). Recently it was shown that the time constant Tau is affected by Pulmonary Arterial Wedge Pressure (PAWP), and thus not constant under all conditions (3).

We therefore questioned how the product $\text{PVR} \times \text{TAC} = \text{Tau}$ depends on PAWP. **Methods:** We have studied proportionality of pressures in a group of patients ($n = 1054$) and determined the contribution of Pulmonary Arterial Wedge Pressure.

Results: We found that sPAP = 1.61mPAP and dPAP = 0.62mPAP, for all PAWP between 1 and 31 mmHg. Calculating PVR and TAC in the standard way as $\text{PVR} = (\text{mPAP} - \text{PAWP}) / \text{CO}$ and $\text{TAC} = \text{PP} / \text{SV}$, with CO: Cardiac Output, PP: Pulse Pressure, SV: Stroke Volume, and HR: Heart Rate, it follows that: $\text{PVR} \times \text{TAC} = (1 - \text{PAWP} / \text{mPAP}) / \text{HR} \times \text{Eq. 1}$

Comparison with Tedford's data (their fig 3C) is as follows:

PAWP Tau-TedfordTau-Eq. 1

6 mmHg 0.43s 0.48s

45 mmHg 0.18s 0.18s

Conclusions: These findings imply that for a certain PAWP and Heart Rate a hyperbolic relation remains, but the time constant Tau depends on the ratio of PAWP/mPAP and Heart Rate. A clinically measured low Tau could suggest a high PAWP.

References

- Lankhaar JW, Westerhof N, Faes TJ, Gan CT, Marques KM, Boonstra A, van den Berg FG, Postmus PE, Vonk-Noordegraaf A. Pulmonary vascular resistance and compliance stay inversely related during treatment of pulmonary hypertension. *Eur Heart J.* 2008; 29:1688-1695.
- Syyed R, Reeves JT, Welsh D, Raeside D, Johnson MK, Peacock AJ. The relationship between the components of pulmonary artery pressure remains constant under all conditions in both health and disease. *Chest.* 2008; 133:633-639.
- Tedford RJ, Hassoun PM, Mathai SC, Girgis RE, Russell SD, Thiemann DR, Cingolani OH, Mudd JO, Borlaug BA, Redfield MM, Lederer DJ, Kass DA. Pulmonary capillary wedge pressure augments right ventricular pulsatile loading. *Circulation.* 2012; 125:289-297.

5.1

MILD REDUCTION OF GLOMERULAR FILTRATION RATE IS ASSOCIATED WITH INCREASED SYSTEMIC VASCULAR RESISTANCE INDEPENDENT OF CHANGES IN CARDIAC AUTONOMIC TONE

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Objective: Our aim was to evaluate the influence of mild impairment in kidney function on hemodynamics and cardiac autonomic tone.