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THE DESIGN OF AN OPTIMAL ARTERIAL NETWORK

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analyze arterial stiffness assessment techniques in varying biomechanical conditions as well as to investigate new imaging approaches and signal processing.

Career Development Lecture

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DIABETES CONFERS A GREATER EXCESS RISK CARDIOVASCULAR DISEASE IN WOMEN THAN IN MEN: CURRENT EVIDENCE, POTENTIAL MECHANISMS, CLINICAL IMPLICATIONS, AND FUTURE DIRECTIONS

S. Peters

University of Oxford, UK

A lack of sex-specific data from early epidemiological studies has typically led to the assumption that the associations between risk factors and disease outcomes are equivalent in women as in men. But increasingly, evidence to support the existence of clinically meaningful sex differences in the relationships between certain risk factors, such as smoking and diabetes with chronic disease is becoming apparent – often to the detriment of women. Determining reliably whether there are clinically meaningful sex-differences in risk factor-disease associations is important, not solely to better understand the aetiology of CVD, but also from a population and public health vantage. Current estimates of the burden of CVD, that are used to inform public health policy, assume that these risk factors effect cardiovascular risk similarly in women as in men. However, if this assumption is proven to be invalid then it would necessitate the revision of the estimates to more accurately reflect the true nature of the relationships in women and men. Moreover, just as possible racial differences in the relationships between risk factors and diseases are considered when tailoring specific interventions for different communities, so could information on important sex differences be used to provide an added impetus for targeted interventions aimed at the treatment and management of these risk factors in both sexes.

Recently we have conducted two systematic reviews and meta-analyses of the sex-specific effects of diabetes on risk of stroke and coronary heart disease. Both studies suggested that women with diabetes had a substantially greater excess risk compared with their male equivalents, even after consideration of differences in baseline levels of other major risk factors. In this talk, the results from these studies will be presented, potential biological, behavioral, or social mechanisms involved will be discussed, clinical implications will be considered, and directions for future research will be provided.

Invited Lecture

CEREBRAL CIRCULATION & COGNITION IN THE ELDERLY

G. J. Biessels

University Medical Center, Utrecht, The Netherlands

Vascular disease is an important cause of cognitive decline and dementia. Approximately 20% of patients with a stroke develop dementia within a year after the event. Even more often, cerebrovascular disease is involved in cognitive decline or dementia in people without an obvious history of stroke. Autopsy studies identify vascular pathology in the majority of patients with dementia, also in those with a clinical diagnosis of Alzheimer's disease. The concept "Vascular cognitive impairment" (VCI) has been introduced as an umbrella term to capture all forms of cognitive impairment – regardless of severity or cognitive profile – that are associated with and presumably caused by cerebrovascular disease. Hence, VCI is heterogeneous, both with regard to aetiology and course of development, ranging, for example, from an acute strategic brain infarct to insidious diffuse white matter pathology.

Importantly, causes of VCI may not be restricted to vascular brain lesions. Abnormalities in vascular function, resulting in altered cerebral haemodynamics, may also be involved, and might represent a potentially modifiable cause of cognitive dysfunction. Currently, the role of haemodynamics in VCI is addressed in a Dutch multidisciplinary research program, called "The Heart-Brain connection". This program addresses the following questions. 1) To what extent do hemodynamic changes contribute to VCI? 2) What are the mechanisms involved? 3) Does improvement of the hemodynamic status lead to improvement of cognitive dysfunction?

In my presentation I will provide background on VCI, review evidence for links between haemodynamics and cognition and introduce the research program of the Heart-Brain connection consortium.

Invited Lecture

MOLECULAR MECHANISMS OF ARTERIAL STIFFENING: ROLE OF VASCULAR SMOOTH MUSCLE CELLS

P. Lacolley

Vandoeuvre-les-nancy, France

Vascular Smooth Muscle Cells (VSMCs) are the stromal cells of the vascular wall, continually exposed to mechanical signals and biochemical components generated in the blood compartment. They are involved in all the physiological functions and the pathological changes responsible for arterial stiffening. Due to their contractile tonus, VSMCs of resistance vessels participate in the regulation of blood pressure and also in arterial stiffness. VSMCs of conduit arteries respond to hypertension-induced increases in wall stress by an increase in cell protein synthesis and extracellular matrix secretion. These responses are mediated by complex signaling pathways, mainly involving RhoA and extracellular signal-regulated kinase1/2. Serum response factor and miRNA expression represent main mechanisms controlling the pattern of gene expression. A progressive decrease in plasticity and reprogramming potential of VSMCs plays a complementary role contributing to the increase in arterial stiffness and associated cardiovascular risk factors in old humans. These key signaling pathways have become the focus of modern aging research and will undoubtedly provide a rich resource for the development of selective drugs interfering with either of these processes and prevention of the number one cause of death in the modern world.

Invited Lecture

MODELLING THE ARTERIAL SYSTEM: BIOMECHANICS OF CENTRAL ARTERY STIFFENING

J. D. Humphrey

Yale University, New Haven, CT, USA

Central arterial stiffening is both an indicator and an initiator of cardiovascular disease, and aging is a ubiquitous cause of stiffening. In this talk, we will discuss the utility of biomechanical models in understanding particular effects of arterial stiffening on systemic hemodynamics and we will discuss advantages of using mouse models to obtain detailed longitudinal information on regional variations in arterial wall properties. In particular, we will focus on delineating intrinsic material and structural stiffness as a function of location along the aorta and we will show results from 3-D computational simulations of the hemodynamics that account for interactions between the blood and regional wall properties. Amongst the different findings, one emerging concept is that adaptive responses appear to favor the maintenance of material stiffness near normal values while offsetting increased hemodynamic loads or genetic defects with changes in structural stiffness. If true, such a response would have important mechanobiological implications.

Related Articles

Bersi MR, Ferruzzi J, Eberth JF, Gleason RL, Humphrey JD (2014) Consistent biomechanical phenotyping of common carotid arteries from seven different genetic, pharmacological, and surgical mouse models. *Annl Biomed Engr* 42: 1207-1223.

Roccabianca S, Figueroa CA, Tellides G, Humphrey JD (2014) Quantification of regional differences in aortic stiffness in the aging human aorta. *J Biomech Behavior Biomed Matl* 29: 618-634.

Invited Lecture

THE DESIGN OF AN OPTIMAL ARTERIAL NETWORK

A. D. Hughes

University College London

The arterial circulation is a network that delivers oxygen and nutrients to cells. Blood flow is achieved by means of a muscular pump but diffusion plays a key role at a cellular level necessitating a branching structure where no cell is more than ~25microm from a capillary.¹

The design of the cardiovascular system is subject to a variety of 'constraints' and 'costs'. It has been postulated that the design of the arterial network might be understood in terms of the need to minimize competing 'costs' within the context of physical or material limits to the system.² These designs can also be envisaged as being subservient to space filling or fractal considerations.³ The signalling mechanisms underlying these

designs remain to be fully characterised, although shear stress, wall tensile stress and metabolic stimuli are likely candidates.^{4,5} I will also review evidence that deviations from a minimal cost condition or optimal design may provide both a measure of disease severity and insights into the underlying disease mechanism.

1. Beard DA, Bassingthwaite JB. Modeling advection and diffusion of oxygen in complex vascular networks. *Annals of biomedical engineering*. 2001;29:298-310
2. Murray CD. The physiological principle of minimum work: I. The vascular system and the cost of blood volume. *Proceedings of the National Academy of Sciences of the United States of America*. 1926;12:207-214
3. Zamir M. Arterial branching within the confines of fractal l-system formalism. *Journal of General Physiology*. 2001;118:267-275
4. Sherman TF. On connecting large vessels to small. The meaning of murray's law. *The Journal of general physiology*. 1981;78:431-453
5. Pries AR, Reglin B, Secomb TW. Remodeling of blood vessels: Responses of diameter and wall thickness to hemodynamic and metabolic stimuli. *Hypertension*. 2005;46:725-731

Invited Lecture

NO GENERATION, BLOOD PRESSURE AND VASCULAR STIFFNESS: LESSONS FROM THE ANGIOTENSIN AT2 RECEPTOR

T. Unger

Cardiovascular Research Institute Maastricht, The Netherlands

Vascular remodeling participates in the development and progression of cardiovascular conditions such as hypertension, atherosclerosis or aneurysm. This process is fine-tuned by neuro-humoral regulatory pathways: the renin-angiotensin system (RAS), being one of the most important. Chronic RAS activation, via AT1 receptor (AT1R) stimulation sets on a series of pro-proliferative, pro-fibrotic, pro-inflammatory signals that promote vascular remodeling and lead to adverse cardiovascular outcomes. The prevention of these outcomes after the blockade of this "deleterious" RAS might be at least in part mediated by the activation of the "protective" RAS. The "protective" RAS involves the AT2 receptor (AT2R) with anti-proliferative, anti-fibrotic, anti-inflammatory and anti-oxidant effects. Some of these protective actions of AT2R stimulation are mediated by AT2R-induced NO generation. Stimulation of AT2R with the new selective, orally active AT2R agonist, Compound 21, in L-NAME hypertensive rats reduced vascular stiffness (pulse wave velocity) and induced vascular structural improvements without lowering blood pressure. These effects cannot be ascribed to NO generation. Alternative effector pathways include activation of protein phosphatases that inactivate the pro-fibrotic MAPKs or anti-apoptotic Bcl-2, down-regulation of MAPKs with NADPH oxidase inhibition and subsequent attenuation of oxidative load, inhibition of NF- κ B activity by epoxidation of 11,12-epoxy-eicosatrienoic acid, direct and indirect anti-inflammatory action with augmented IL-10 production and T cell differentiation, and, finally, heterodimerization of the AT2R with AT1R that abrogates the AT1R-dependent pro-fibrotic effects.

McDonald Lecture

CROSS-SECTIONAL ARTERIAL MECHANICS: THE RENAISSANCE

S. Laurent

INSERM U970 and Paris-Descartes University, Paris, France

These last years, the widespread use of regional pulse wave velocity in clinical practice has overlooked the usefulness of local arterial stiffness. Indeed, the elastic properties of large superficial arteries (carotid, femoral, brachial and radial) can be assessed locally through the systolic-diastolic variations in arterial lumen diameter and thickness using high resolution echotracking systems, and local pulse pressure using aplanation tonometry. The mechanical properties of deep arteries like the thoracic aorta can be assessed using cine magnetic resonance imaging (MRI).

The aim of this review is to discuss how the measurement of the geometrical and functional properties of large arteries contributed to important conceptual achievements in arterial mechanics. Several aspects are discussed that concern the pathophysiology, pharmacology and epidemiology of arterial stiffness. We explain (1) how the precise phenotyping of the changes

in large and small artery during essential hypertension can enter a vicious circle of aggravation named large/small artery cross-talk; (2) how the understanding of the wall material elastic properties that are associated with arterial wall hypertrophy in essential hypertension, has led to the discovery of putative novel mechanisms involved in arterial stiffness; (3) how local measurements of arterial stiffness can help to find the true pathway followed by the pressure wave, when a single-site measurement/arm cuff oscillometric method is used; (4) how the study of arterial remodeling and mechanics during long-term antihypertensive treatment can unmask a blood-pressure independent reduction in arterial stiffness; and, finally (5) how carotid stiffness can predict cardiovascular events independently of regional pulse wave velocity.

Debate

CENTRAL PRESSURE SHOULD BE USED IN CLINICAL PRACTICE

J. Sharman

Hobart, Australia

The original purpose for developing the technique to record brachial blood pressure (BP) more than 100 years ago was to estimate aortic (central) BP. While high brachial BP is an important cardiovascular risk factor, it is clear that major differences in central systolic BP (SBP; e.g. >30 mmHg) can occur among people with similar brachial SBP. It is also proven that central SBP responses to antihypertensive therapy can differ substantially from brachial SBP responses, such that true treatment effects cannot be gauged from conventional brachial BP. Importantly, assessment of central BP results in: 1) improved predictive accuracy of future cardiovascular events beyond brachial BP and other cardiovascular risk factors; 2) superior diagnostic accuracy over brachial BP and; 3) different patient management than usual care guided by brachial BP. Collectively the above data satisfy criteria for central BP being a better cardiovascular risk biomarker than brachial BP. As with all medical advances there are areas of research need and international consensus is required on issues such as standardization of techniques. However, central BP can now be accurately estimated (with appropriate waveform calibration) using brachial cuff methods in an approach that is familiar to clinicians, acceptable to patients and amenable to widespread use. In other words, this modern BP technique finally satisfies the original purpose for measuring BP as intended more than 100 years ago. Although the tipping point towards routine use is yet to be reached, the body of evidence continues to favour the view that central BP should be used in clinical practice.

Debate

CENTRAL PRESSURE SHOULD BE USED IN CLINICAL PRACTICE

G. Mitchell

Norwood, USA

The heart, brain and kidneys are key targets of pulsatile damage in older people and in patients with longstanding hypertension. These central organs are exposed to central systolic and pulse pressures, which may differ from the corresponding peripheral pressures measured in the brachial artery. Studies employing the generalized transfer function as a means to estimate central pressure have demonstrated a large difference between central and peripheral systolic and pulse pressure that diminishes with age but remains substantial even in octogenarians. As a result of this persistent difference, some have advocated that central pressure may represent a more robust indicator of risk for target organ damage and major cardiovascular disease events. From the perspective of risk prediction, it is important to acknowledge that a new technique must add incremental predictive value to what is already commonly measured. Thus, in order to justify the added complexity and expense implicit in the measurement, central pressure must be shown to add significantly to a risk factor model that includes standard cardiovascular disease risk factors. A limited number of studies have shown marginally better correlations between central pressure pulsatility and continuous measures of target organ damage in the heart. A similarly limited number of prospective studies in unique cohorts have suggested that central pressure may provide marginally better risk stratification, although no reclassification analysis has been published. Thus, currently available evidence does not provide sufficient justification for widespread adoption and routine use of central pressure measurements in clinical practice.