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Personalising hypertension treatment?

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Running title: Personalising hypertension treatment?

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"It's far more important to know what person the disease has than what disease the person has" – Hippocrates (c. 460 BC – c. 370 BC)

There is a pressing need to personalise cardiovascular disease prevention and nowhere more so than in treating hypertension[1]. Hypertension should no longer be treated as an individual disease, but in the context of a patient's total cardiovascular risk; new guidelines [2] may lead to half of the American population being considered for drug therapy to lower blood pressure, but if there were ways to identify those who would benefit; this number might be reduced greatly with considerable cost savings. One approach would be to look for evidence of target organ damage and use this as additional reason for starting treatment. The prognostic impact of regressing vascular structural alterations for a number of cardiovascular and metabolic diseases is a clinical priority. Understanding the significance of the microcirculation and how even small architectural changes can impact on normal physiological processes underlies the importance of this system as a potential tool to add to making clinical judgements. The past 25 years of research in the field has identified some key principles; (i) the significance of the microcirculation on the regulation of blood pressure [3, 4] (ii) that these vessels undergo active and adaptive remodelling to long term haemodynamic changes [5] (iii) remodelling of resistance arteries can be categorised as inward eutrophic (rearrangement of otherwise normal material around a narrowed lumen) or inward hypertrophic remodelling (vascular smooth muscle cell hypertrophy or hyperplasia) [6] (iv) the increase in the media-to-lumen ratio linked with remodelling is a powerful predictor of cardiovascular events [7].

Despite consistent research over the past 25 years seeking to understand the mechanisms by which remodelling occurs, very few contribute to the translational power that is gained in understanding how they contribute to vascular normality. Using a disease-centred tool in which individuals have one single condition is not appropriate for the array of cardiovascular diseases of which patients are at risk if indeed the current understanding is correct.

However, defining normality is a problem; non-modifiable risk factors including sex, age and ethnicity change what is 'normal', yet very few studies factor this in to their prognostic calculations. This shift in thought is supported by a recent study by Puato and colleagues which highlights that accurate phenotyping of the cardiovascular risk profile of each patient, alongside a patient-tailored pharmacological approach is the most effective strategy to limit vascular damage and associated cardiovascular risk [8]. Therefore it is perhaps unsurprising that the current day research has experienced a move to 'personalise' prognostic tools based on remodelling measures to enhance their usability in the clinical setting, thus delivering more patient-centred care.

The research from this group has made significant contributions in terms of our overall understanding of how vascular remodelling is linked to hypertension. In this issue of the Journal, Bruno and colleagues seek to establish age- and sex-specific reference values for media to lumen ratios in small arteries [1]. In a multi-centre study, Bruno and colleagues have recruited almost 300 patients, 91 of whom were healthy, and have presented the largest cohort of data collected through myography assessment. Using resistance arteries found in abdominal or gluteal biopsies, the authors have performed statistical analysis to assess media to lumen ratios and have calculated age and sex-specific reference intervals for healthy individuals. They then examined whether these were affected by significant cardiovascular risk factors including BMI, fasting blood glucose, smoking status, systolic blood pressure and total cholesterol. From these data, Bruno et al. propose that these values will be helpful for the further investigation of cardiovascular risk factors in microvascular damage and any associated organ damage, as well as allowing for the effectiveness of treatments to be ascertained. As well as establishing age and sex specific reference values, this paper sets out some thought provoking insights into alternative remodelling routes which occur in the presence of complex cardiovascular risk factors when gender is considered. The authors acknowledge that there are limitations to the study; microcirculatory endothelial function was not examined, which itself is strongly associated with cardiovascular events but not necessarily due to changes in media to lumen ratio [9], furthermore, any change in reference values due to ethnicity is likely to require further studies [1].

The clinical impact of these findings could be phenomenal. However, the translation of these measures is limited by the very nature in which they are taken; the invasiveness required precludes this from being a valuable clinical resource and a way of looking closely at the microcirculation *in vivo* is needed urgently. Maybe assessing retinal arteries under standardised conditions is the way forward [10], however until a prognostic value of non-invasive measures of microvascular structure is made, progression is somewhat limited [11]. What can be taken from this study is that we cannot see patients as being the same: normality cannot be assumed. In an era where we are moving progressively towards personalised medicine, the Bruno group is making small, yet important steps, in personalising cardiovascular medicine for improved outcomes and patient care. We wait with keen anticipation for their next studies in this field.

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