reliable. In this respect we should make clear that our data comparing males and females are presented using the β index simply to permit a comparison with the results of Rydén Ahlgren et al.

Finally, in the Discussion section the authors [1] referring to differences between central aortic and peripheral BP write "no significant age or gender-related differences are seen thus allowing comparisons between individuals and groups". Surely part of the issue here is whether the differences between intra-aortic BP and brachial BP change with diabetes status? We are not aware of any work comparing such measurements in diabetic and non-diabetic individuals. Thus, we have another variable which may be different between the control and diabetic cohorts studied and which needs to be considered. Given this, we simply do not know whether the authors' assumption that sphygmomanometrically measured BP in the brachial artery can be reliably substituted for the aortic BP at a single aortic cross-section in both diabetic and non-diabetic subjects is valid. To us this appears to be another compelling reason to report the 'raw', measured distensibility data ($\Delta D/D_d$) rather than a derived parameter such as β .

Yours sincerely,

E. D. Lehmann, K. D. Hopkins, R. G. Gosling

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Increased arterial stiffness in IDDM women – methodological considerations

Dear Sir,

We are pleased to learn of the interest Dr. Lehman et al. show in our recent paper.

In this paper stiffness (β) data were presented as an expression of arterial distensibility. As suggested by Dr. Lehman et al. also the strain (fractional diameter change) = $\frac{\text{systolic diameter} - \text{diastolic diameter}}{\text{diastolic diameter}}$ of the abdominal aorta

now is shown (Fig. 1). As can be seen, the aortic strain is significantly lower in women ($p = 0.0025$), but not in men ($p = 0.9$) with insulin-dependent diabetes mellitus (IDDM), as compared with healthy control subjects of corresponding age and sex, confirming the earlier presented β results. However, strain is not only dependent on the vessel wall constituents but also on the distending force, that is, the blood pressure. The pressure/diameter relationship of the aorta is curvilinear as is evident from simultaneous recordings of arterial pressure and diameter with a more distensible part at lower than at higher pressures. Although there is no sharp inflection point in the curve, the transition from distensible to stiff behaviour occurs above 80 mm Hg [1]. These mechanical characteristics have been attributed to the properties of the matrix in the wall, mainly elastin and collagen. The more distensible elastin is the principle load bearer at low pressures and small distensions, whereas both elastin and the stiffer collagen are load-bearing at high pressures and large distensions [2]. Thus, changes in mean distending pressure (MAP) and pulse pressure affect the aortic distensibility as well as the pulse wave velocity (PWV). In Figure 1 it can be seen that the strain in healthy control subjects decreases with age. However, MAP as well as pulse pressure

Fig. 1. Aortic strain (fractional diameter change) in women and men with IDDM. The lines represent mean, upper and lower of 95 % CI, for the control women and men. Note the significantly decreased strain in women, but not in men with IDDM ($p = 0.0025$ and $p = 0.9$, respectively)

increase and in a different manner in women and men. This indicates that, if you use strain as an index of distensibility, the decrease with age surely is underestimated and, furthermore, sex-specific changes might be lost. Therefore, the blood pressure is essential and cannot be neglected. The β was designed to characterise the entire deformation behaviour of the arterial wall without pressure dependence in the physiologic range = $\ln(\text{systolic pressure}/\text{diastolic pressure})$. This was tested in healthy control subjects, men and women separately, both at young and older age by comparing the β index of the abdominal aorta at rest and during isometric exercise, increasing MAP about 40 to 50 %. β showed a slight tendency to increase, however, this failed to reach statistical significance [3]. Furthermore, the entire cohort of healthy normotensive control subjects (85 women and 84 men, range 4 to 80 years) was analysed by use of a multiplicative multiple stepwise linear regression model concerning the influence of age, aortic diameter and blood pressure on aortic β . β was influenced most by age in both men (91 %, $p < 0.0001$) and women (75 %, $p < 0.0001$), and only to a small extent by diameter (men 1 %, $p < 0.01$, women 3 %, $p < 0.01$), whereas blood pressure analysed with respect to systolic pressure, MAP, pulse pressure, $\ln(\text{systolic pressure}/\text{diastolic pressure})$ had no influence. The optimal method of measuring the blood pressure is at the site of diameter measurements. However, this is impractical in larger series, and is why in several studies indirect registrations of the brachial pressure have been used as an approximation of the aortic pressure. This assumption neither takes into account the difference in pressure between central and peripheral arteries, which is attributed to wave travel and reflection within the arterial tree [4], nor the possible error when estimating the brachial arterial pressure non-invasively instead of invasively. These problems were addressed in a recent study in our laboratory, where the intraarterial pressure in the abdominal aorta was measured simultaneously with non-invasively measured brachial pressure. Together with the corresponding aortic diameter changes β was calculated. No differences in systolic pressure were seen, but the diastolic pressure was slightly higher when determined by auscultation than when measured directly in the aorta. No age or sex-related differences were observed. This leads to a slight systematic underestimation of β [1]. The problem, whether the non-invasive measurement of brachial blood pressure might be erroneous selectively in the diabetic population, deserves some attention, since this has been shown in ankle

blood pressure measurements [5]. However, to our knowledge no similar findings have been reported in the upper arm. Furthermore, the similar stiffness and strain values, with a selective change in the IDDM women as compared with control subjects, speak against this assumption. Dr. Lehman et al. discuss the relation between stiffness and blood pressure in their diagram. In our opinion, no conclusions can be drawn from this, as the values seem not to be corrected for the relation between stiffness and age. A multiple regression analysis in our IDDM patients shows the same findings as in the healthy control subjects, that is, β is influenced by age in both men ($p < 0.0001$) and women ($p < 0.0003$), whereas blood pressure analysed with respect to systolic pressure, MAP and diastolic pressure have no significant influence. Thus, we feel that the β index is a reliable tool to use in the study of aortic wall mechanics.

In conclusion, we have shown an increased arterial stiffness in women, but not in men, with IDDM. This is confirmed by the fractional diameter change (strain). This may be a pathogenic factor which could help to explain the gender-related differences in the risk for cardiovascular complications in diabetic subjects.

Yours sincerely,
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