Endothelial dysfunction in hypertensive patients and in normotensive offspring of subjects with essential hypertension

Essential arterial hypertension (EH) is an important risk factor for atherosclerosis. There is growing evidence that endothelial dysfunction is the earliest event in atherogenesis and also precedes morphological changes of the arterial wall in hypertensive patients. One of the most widely recognised methods of determining the endothelial function is the brachial artery dilatation (FMD) of the brachial artery is also used non-invasively whether flow-mediated dilation capability of systemic conduit arteries. On the other hand, there is only little evidence, albeit controversial, of the resistance arteries. In contrast to hypertensives with well documented elevated blood pressure (>145/95 mm Hg in a sitting position in at least three different measurements before starting treatment) were included. The hypertensive subjects took their medication (either long acting calcium channel antagonists or angiotensin converting enzyme (ACE) inhibitors) 6–8 hours before haemodynamic measurements were performed. The second group of 44 healthy normotensive subjects (32 men and 12 women), matched with the patients in age and sex, served as controls. The third group comprised 41 subjects (23 men and 18 women, mean age 25 years), with a family history of essential hypertension in their first degree relatives (parents or siblings, or both). In the fourth control group there were 41 volunteers with age and sex matched with FT subjects, and without a family history of hypertension. Both groups of young volunteers had recorded normal blood pressure at least three times in the year preceding the investigation. Information on blood pressure was obtained from family doctors and their medical records.

The dilation capability of the brachial artery was studied by high resolution ultrasound. The method of haemodynamic measurements was described elsewhere. The relative flow increase during reactive hyperaemia was calculated as the maximum flow divided by the flow during rest. The FMD response was expressed as a change in the end diastolic diameter of the brachial artery during reactive hyperaemia compared to the baseline measurement, and used as a measure of endothelium dependent vasodilation. Endothelium independent vasodilation of the brachial artery was studied by way of the sublingual application of 0.5 mg glyceryl trinitrate (GTN).

The patients with EH had significantly higher systolic and diastolic blood pressure than the controls (140.76 (11.74) mm Hg v 122.52 (8.11) mm Hg, p < 0.00005) and a higher body mass index in comparison to the baseline measurement, and used as a measure of endothelium dependent vasodilation. Endothelium independent vasodilation of the brachial artery was studied by way of the sublingual application of 0.5 mg glyceryl trinitrate (GTN).

In EH patients the blood pressure was higher in FT patients than in the controls (fig 1), and GTN induced dilation was comparable between the FT group and the controls (476 (129)% v 444 (140)%), p = 0.099. FMD in hypertensives was significantly less than in controls (fig 1), and GTN induced dilation was as well (12.1 (4.3)% v 16.1 (4.6)%, p = 0.00007). FMD in hypertensive patients was also impaired when corrected for the GTN response (2.9 (3.0)% v 7.7 (2.4)%, p < 0.00005). In subjects with FMD was also decreased in comparison to controls (fig 1); in contrast to hypertensives, the GTN induced dilation was comparable between the groups of young volunteers (14.0 (3.3)% v 15.7 (5.2)%).

In the group of older participants as a whole, the univariate analysis FMD was strongly inversely related to the systolic and diastolic blood pressure (r = −0.27, p = 0.045), to the duration of hypertension (r = −0.24, p = 0.00005), and the body mass index (r = 0.27, p = 0.010). The systolic blood pressure and the body mass index (p < 0.00005), yet weakly related to the age (p = 0.045). There was also a strong inverse relation observed between the dilation capability (flow and GTN mediated) and the baseline vessel diameter (p < 0.00005). In contrast, hyperaemic flow increase was not a significant predictor of FMD. Variables that were significant in the univariate analysis were included in different multiple regression models. Multivariate analysis showed that in patients with EH the FMD was related to the family history of hypertension (partial r = −0.42, p < 0.00005), the systolic blood pressure (partial r = −0.43, p < 0.00005), and the baseline vessel diameter (partial r = −0.27, p = 0.010).

The significant model (p < 0.00005) with a relatively high goodness of fit (R² = 0.53). Similar results were obtained when diastolic blood pressure was substituted for the systolic blood pressure. In both groups of young subjects (FT plus controls), FMD was strongly negatively related to the family history of hypertension (p = 0.00005). FMD was also negatively related to the baseline vessel diameter (p = 0.002). Multivariate regression analyses including the family history of hypertension, the baseline vessel diameter, the body mass index (p < 0.00005), and the systolic blood pressure (p = 0.030), revealed that the family history of hypertension (partial r = −0.42, p = 0.0002) and the baseline vessel diameter (partial r = −0.24, p = 0.048) were the most important determinants of FMD (R² = 0.37, p < 0.00005).

The present study demonstrated that, in spite of treatment, hypertensives without cardiovascular events showed decreased FMD of the brachial artery as compared to the normotensive controls. This difference was also preserved after making corrections.
findings indicate that hypertension is related to endothelial and smooth muscle cell dysfunction. Endothelial dysfunction precedes the manifestation of hypertension and is present in the offspring of subjects with EH.

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Quality of life in patients with silent atrial fibrillation

Atrial fibrillation (AF) is a common arrhythmia associated with substantial morbidity, mortality, and health care cost. Although AF is responsible for a variety of symptoms, at least one third of patients report no overt symptoms and are unaware of their arrhythmic condition. This silent AF is diagnosed incidentally during routine physical or electrocardiographic examination. In some cases, asymptomatic AF is revealed only after complications such as stroke or congestive heart failure have occurred. Implantable pacemakers or defibrillators equipped with long term Holter memory function have shown that a very large proportion of patients (>50%) have unsuspected episodes of silent AF. Silent AF is likely to be associated with morbidity and mortality rates similar to those in symptomatic AF, but its effect on quality of life (QoL) has not yet been established. We studied 154 patients: 145 paroxysmal (60.5%) or persistent (39.5%) AF. Symptoms relevant for AF were selected from Bubien and Kay's symptom checklist, including palpitations, dyspnoea, dizziness, exercise intolerance, chest discomfort, and syncope.

Table 1: Comparison of quality of life in patients with silent (group 1), symptomatic (group 2), all atrial fibrillation (all AF), and healthy subjects (control)

<table>
<thead>
<tr>
<th>SF-36 score</th>
<th>Group 1 n=38</th>
<th>Group 2 n=116</th>
<th>All AF n=154</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role-physical</td>
<td>88 (28)</td>
<td>83 (26)</td>
<td>35 (30)*</td>
</tr>
<tr>
<td>Vitality</td>
<td>71 (14)</td>
<td>63 (15)</td>
<td>42 (10)*</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>89 (19)</td>
<td>89 (19)</td>
<td>69 (27)*</td>
</tr>
<tr>
<td>Social functioning</td>
<td>92 (14)</td>
<td>87 (23)</td>
<td>67 (27)*</td>
</tr>
<tr>
<td>Mental health</td>
<td>81 (11)</td>
<td>75 (15)</td>
<td>65 (18)*</td>
</tr>
<tr>
<td>Role-emotional</td>
<td>92 (24)</td>
<td>88 (22)</td>
<td>58 (42)*</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>77 (15)</td>
<td>81 (14)</td>
<td>65 (19)*</td>
</tr>
<tr>
<td>General health</td>
<td>78 (18)</td>
<td>63 (17)*</td>
<td>51 (21)*</td>
</tr>
<tr>
<td>Symptom burden (checklist)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom frequency</td>
<td>10 (6)</td>
<td>11 (5)</td>
<td>26 (8)*</td>
</tr>
<tr>
<td>Symptom severity</td>
<td>8 (5)</td>
<td>9 (3)</td>
<td>22 (6)*</td>
</tr>
<tr>
<td>Total functional capacity</td>
<td>93 (11)</td>
<td>90 (11)</td>
<td>71 (20)*</td>
</tr>
<tr>
<td>Global life satisfaction</td>
<td>8.0 (1.2)</td>
<td>7.3 (1.6)*</td>
<td>5.9 (1.9)*†</td>
</tr>
</tbody>
</table>

Data presented as raw mean (SD) scores; *p < 0.003 compared with healthy controls; †p < 0.005 compared with group 1; AF, atrial fibrillation.
perception of general health was significantly poorer in the latter (p < 0.003). Global life satisfaction was significantly decreased in “asymptomatic” patients compared with normal subjects (p < 0.003).

This study suggests that the subjective effects of AF on isolated physical aspects or on social and emotional spheres may be subtle in patients with little or no symptoms, but the arrhythmia may significantly decrease the overall perception of well being in this population. Our data are consistent with the results of other studies evaluating QoL in AF subjects (p < 0.003).

"asymptomatic" patients compared with normal subjects (p < 0.003). Global life satisfaction have also been achieved after atrioventricular node ablation in patients with refractory atrial fibrillation. Even less is known about QoL in patients whose rhythm and/or rate are believed to be well controlled by antiarrhythmic drugs or in those who can be potential candidates for treatment with implantable atrial defibrillators. Although pharmacological treatment may prevent the arrhythmia recurrence, it often renders symptomatic AF to asymptomatic, and the assessment of QoL in these patients may have an impact on the risk-benefit ratio of antiarrhythmic drugs. A serious consideration should be given to QoL in atrial defibrillator recipients as this device may decrease a total symptom burden of AF but usually it does not affect the recurrence of arrhythmia, in particular, short, non-treated episodes which may be well tolerated or may be recognised by a patient as AF.

The issue of long life antiocoagulation also remains open in patients with AF in whom frequent, long lasting, highly symptomatic episodes have been suppressed by either kind of treatment but the arrhythmia has not been completely abolished. This study indicates that several aspects of QoL may be reduced in patients with AF, even in the absence of symptoms of the arrhythmia. QoL should be assessed and treatment for the improvement of QoL should be considered in patients with “asymptomatic” AF.

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