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Early androgenetic alopecia as a marker of insulin resistance

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The previously proven association between androgenetic alopecia and serious cardiovascular events raises a question of the common pathogenetic mechanism of these disorders. Our practice-based case-control study in men aged 19–50 years showed a strikingly increased risk of hyperinsulinaemia and insulin-resistance-associated disorders such as obesity, hypertension, and dyslipidaemia in men with early onset of alopecia (<35), compared with age-matched controls. This finding supports the hypothesis that early androgenetic alopecia could be a clinical marker of insulin resistance

An association between androgenetic alopecia and serious cardiovascular events such as myocardial infarction and fatal ischaemic heart disease has been reported,^{1,2} but the mechanism explaining this association remains unclear. Androgens and genetic susceptibility are essential for the development of androgenetic alopecia, and insulin resistance induced by endothelium dysfunction and inflammation mediators is seen as a main pathogenetic mechanism for atherosclerosis.³ Androgen receptors have been found on the arterial-wall endothelium and on the cardiac muscle of subhuman species, but the direct effects of androgens on the vascular endothelium or vascular function are not well known.⁴ Whether insulin resistance induces or promotes androgenetic alopecia or whether risk factors associated with insulin resistance are more common in people with androgenetic alopecia than those with normal hair or other forms of alopecia, remains to be answered.

We did a practice-based case-control study on patients with early-onset androgenetic alopecia (younger than 35 years) and age-matched controls.

Variable	Cases	Controls	Odds ratio (95% CI)
Body-mass index			
≥27 kg/m ²	66/154 (42.9%)	31/151 (20.5%)	2.90 (1.76–4.79)
≥30 kg/m ²	29/154 (18.8%)	13/151 (8.6%)	2.46 (1.24–4.88)
Medication			
Antihypertensives	35/154 (22.7%)	19/154 (12.3%)	2.09 (1.14–3.82)
Antidiabetics	4/154 (2.6%)	2/154 (1.3%)	2.02 (0.38–10.89)
Lipid-lowering drugs	20/154 (13.0%)	5/154 (3.3%)	4.45 (1.74–11.34)
Clinical characteristics			
Cluster of insulin-resistance risk factors	19/144 (13.2%)	4/130 (3.1%)	4.79 (1.73–13.27)
Insulin concentration >10.0 μU/L	39/87 (44.8%)	26/87 (29.8%)	1.91 (1.02–3.56)

Odds ratios (95% CI) for insulin-resistance-associated cardiovascular risk factors and being on antihypertensive, antidiabetic, or lipid-covering medication

The cases were men aged 19–50 years and identified as having androgenetic alopecia in health-centre visits in a town in Finland with a total population of 7300, including 1253 eligible men of that age-group. We started collecting data on cases on April 1, 1997, and continued until Feb 28, 1999. 154 cases in total were identified. We defined cases as men who had androgenetic alopecia of at least grade III vertex or more on Hamilton's classification scale for alopecia, modified by Norwood,⁵ and that had been present since at least age 35 years. For each case, we selected an individually age-matched control living in the same town from official vital statistics data. 143 (93%) of 154 controls had visited the health centre during the collection period.

Information on diagnoses of chronic diseases and data on current medication, weight and height, fasting total cholesterol, triglycerides, HDL cholesterol, and blood glucose were collected from patients' records, and if data were not available, participants were invited for clinical investigation and laboratory tests. We took blood samples to measure insulin by EIA from 229 participants (125 cases and 104 controls) among whom were 87 entire case-control pairs. Cases and controls who did not have insulin measurements did not differ for laboratory data and anthropometric measures. We made a cluster of the following insulin-resistance-associated risk factors: dyslipidaemia (HDL cholesterol <0.9 mmol/L, triglycerides ≥1.7 mmol/L, or lipid-lowering medication), abnormal glucose metabolism (fasting blood glucose ≥6.7 mmol/L twice or antidiabetic medication), body-mass index (≥30 kg/m²), and systolic blood pressure (≥160 mm Hg). A cluster was present if at least three variables were simultaneously positive.

We analysed the association of insulin-resistance-associated risk factors with alopecia separately by 2×2 cross tabulations to calculate the odds ratio and 95% CI for each dichotomised variable and for the medications used to treat hypertension, dyslipidaemia, and diabetes.

When we compared the means of laboratory tests and body-mass index between cases and controls, the cases had significantly higher body-mass index (27.1 vs 25.1 kg/m², p<0.0001), but when we compared metabolic parameters, the groups did not differ.

We found a strong association in men with early-onset androgenetic alopecia with being on antihypertensive (p=0.024) and lipid-lowering (p=0.003) medication, as well as being moderately (>27 kg/m², p<0.001) or severely (>30 kg/m², p=0.012) overweight, all of which are effects of metabolic syndromes (table). The participants with alopecia were all younger than 50 years and were more likely to have clustered risk factors than those without alopecia (p=0.004). In addition the risk for hyperinsulinaemia was two-fold in men with alopecia

compared with controls ($p=0.06$). The finding that metabolic parameters did not differ between cases and controls might be due to the higher frequency of use of medication and more intensive counselling for improvement of eating habits and increase in physical activity in cases.

The number of men with at least grade III alopecia identified in our study (154) represents 12% of the total population in the same age-groups. This prevalence of alopecia corresponds roughly to that previously reported among white men in these age-groups. More than 90% of controls had visited the health centre during the data-collection period, which means that they represent the same target population as the cases. No control had alopecia of grade III or more on the Norwood's scale.

Our observations raise the question whether insulin resistance could be a pathophysiological mechanism or promoting factor in early androgenetic alopecia, which could, in turn, be an early marker of insulin resistance. The underlying mechanism that possibly connects insulin resistance and androgenetic alopecia requires further research. However, people with early androgenetic alopecia might benefit from screening for cardiovascular risk factors and for insulin resistance.

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Internal carotid-artery response to 5% carbon dioxide in women with polycystic ovaries

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Although polycystic ovary syndrome is associated with hypertension, hyperlipidaemia, and insulin resistance, mortality from cerebrovascular disease is not increased. We previously reported lower downstream resistance in the internal carotid artery in women with polycystic ovary syndrome. This study was designed to assess vascular reactivity by measuring the response to inhalation of 5% carbon dioxide. We studied 34 young women with polycystic ovary syndrome, 15 with symptomless polycystic ovaries, and 18 controls.

About 20% of women of reproductive age have polycystic ovaries on ultrasonography, and up to half of them will

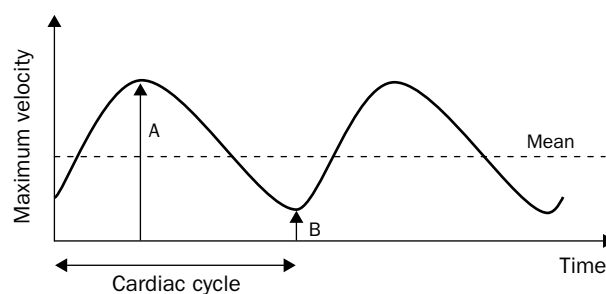


Figure 1: Maximum velocity waveform used in calculation of pulsatility index

A=peak systolic velocity; B=end-diastolic velocity.

have associated symptoms of hirsutism, obesity, menstrual irregularity, or infertility—ie, polycystic ovary syndrome.¹ Recent studies have shown an association between polycystic ovary syndrome and risk factors for stroke (insulin resistance, hypertension, hypercholesterolaemia).² We have previously reported decreased baseline cerebrovascular resistance in polycystic ovary syndrome, independent of body-mass index, blood pressure, insulin resistance, and endocrine factors.³ In the present study, we assessed cerebrovascular reactivity to 5% carbon dioxide (a known cerebral vasodilator) in young women with symptomless polycystic ovaries, women with polycystic ovary syndrome, and healthy controls, by measuring the change in ultrasound variables in the internal carotid artery.

The participants, aged 19–31 years, were 34 women with polycystic ovary syndrome, 15 symptom-free women with evidence of polycystic ovaries on a transvaginal scan, and 18 controls who had normal ovaries on ultrasonography and who had not sought treatment for menstrual disturbances, infertility, or hirsutism at any time. Women who smoked, had known cardiovascular disease, or who took oral contraception or medication that could influence vascular resistance were excluded. Ethics committee approval and written informed consent were obtained.

Doppler scans were done with an Eccocee SSA 340 (Toshiba, Nasu, Japan) at baseline and after inhalation of 5% carbon dioxide for 5 min. The pulsed doppler range gate was placed across the internal carotid artery 2 cm distal to the carotid bifurcation. Ambient noise, lighting, and temperature were controlled throughout. We measured peak systolic velocity, and calculated the pulsatility index from the following formula: (peak systolic velocity minus end-diastolic velocity)/mean velocity throughout cardiac cycle (figure 1). Doppler variables for the right and left

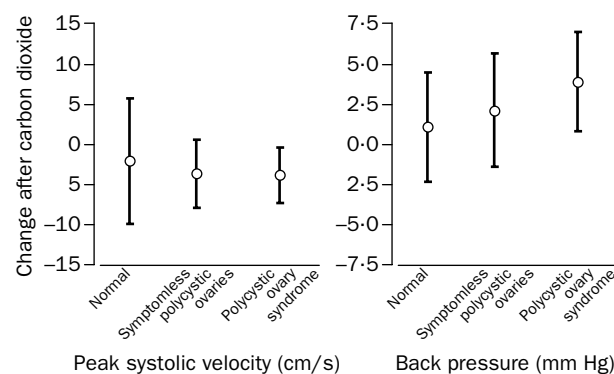


Figure 2: Changes in doppler variables in the internal carotid artery after inhalation of 5% carbon dioxide

Points=mean change, bars=95% CI.