Detection of subclinical atherosclerosis by electron beam tomography in females with heterozygous familial hypercholesterolaemia

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PARTICIPANTS AND METHODS

HeFH was diagnosed using the US MED PED criteria that rely on low density lipoprotein (LDL) cholesterol values and on a previous diagnosis of FH in first and second degree relatives. At the time of evaluation no patient was using lipid lowering drugs. CAC was determined by electron beam tomography with an Imatron C-150 scanner (Imatron Corporation, San Francisco, California, USA) in 27 consecutive HeFH females (10–74 years old, mean 40 years, median 39 years) from the Lipid Outpatient Clinic of the Heart Institute (InCor) and in 71 asymptomatic normolipidaemic females from the Preventive Medicine Centre of the Albert Einstein Hospital (34–68 years old, mean 47 years, median 46 years).

RESULTS

Table 2 shows that HeFH patients were younger and had a lower prevalence of smokers and former smokers than normal women. Total cholesterol, LDL cholesterol, and plasma triglycerides were higher in HeFH women compared to normal women. Figure 1 shows the distribution of calcium scores in HeFH and in normal women. There was a greater prevalence of CAC in the HeFH group than in the normal women (51.8% (n = 14) and 16.9% (n = 12), p = 0.0009, respectively), corresponding to a relative risk of 3.07 (95% confidence interval (CI) 1.5 to 6.2). The prevalence of CAC was higher in HeFH than normal: 66.0 (95% CI 18.0 to 113.0) vs 11.0 (95% CI 1.5 to 20.0), p = 0.004. Also, the prevalence of severe CAC was greater in HeFH than in normals (100% (n = 14) and 66.6% (n = 8), p = 0.03) corresponding to a relative risk of 2.3 (95% CI 1.42 to 3.82) of those HeFH females with severe

Abbreviations: CAC, coronary artery calcification; CI, confidence interval; CHD, coronary heart disease; FH, familial hypercholesterolaemia; HeFH, heterozygous familial hypercholesterolaemia
CAC. 5 (57.1%) were at reproductive age (< 45 years old). The cholesterol–age product (mmol–year/l) was greater in HeFH than in normal women (277.4 (176.0) and 146.0 (52.0), respectively, p < 0.0001) and it was correlated with CAC in HeFH but not in normal women (respectively r² = 0.46, p = 0.0002, and r² = 0.0081, p = 0.21).

DISCUSSION

In this study females with HeFH had a greater prevalence and severity of subclinical atherosclerosis as determined by electron beam tomography than normal women. Electron beam tomography could be useful to stratify the risk of CHD in these patients since CAC correlates with atherosclerotic plaque burden and with the risk of clinical events.1 The detection of severe subclinical atherosclerosis would warrant initiation of aggressive statin treatment in these women, mainly in those with disease diagnosed at an early age. Studies performed in non-FH patients showed that subjects with severe subclinical atherosclerosis2 have a risk of CHD events greater than the 2% annual threshold chosen to start statin treatment by the joint task force of European and other societies on coronary prevention.3 In non-FH subjects the absence of CAC indicates a very low risk of clinical CHD events in the short and medium term, even in the presence of CHD risk factors.4 However, other risk factors such as smoking, hypercholesterolaemia, and hypertension have also been associated with the intensity of CAC. Despite being younger and having a lower prevalence of smokers and former smokers, HeFH women had a greater prevalence and severity of CAC than normal women. The exposure to high cholesterol concentrations during their lifetime, as shown by the increased cholesterol–age product and its correlation with CAC, in HeFH patients but not in normal women, is certainly associated with this finding. Our results are in accord with previous studies performed in children and young adults as well as in homozygous FH patients who showed a correlation of cholesterol–age product and intensity of CAC.5 6 The greater prevalence of severe CAC in HeFH is in accord with the high and early prevalence of clinical CHD in HeFH.7 8

In conclusion, HeFH females had a higher prevalence and greater intensity of CAC than normal women. Electron beam tomography might be helpful in identifying female subjects with early onset and severe subclinical atherosclerosis, and might also help in deciding when to start lipid lowering treatment with statins.

Another potential use of electron beam tomography in HeFH patients would be for following up disease progression—that is, calcification—and for evaluating the effectiveness of lipid lowering treatment in modifying the course of the disease.

In non-FH subjects the intensity of CAC is greater in men than women, and age is the most important determinant of CAC presence and severity.1 9 However, other risk factors such as smoking, hypercholesterolaemia, and hypertension have also been associated with the intensity of CAC. Despite being younger and having a lower prevalence of smokers and former smokers, HeFH women had a greater prevalence and severity of CAC than normal women. The exposure to high cholesterol concentrations during their lifetime, as shown by the increased cholesterol–age product and its correlation with CAC, in HeFH patients but not in normal women, is certainly associated with this finding. Our results are in accord with previous studies performed in children and young adults as well as in homozygous FH patients who showed a correlation of cholesterol–age product and intensity of CAC.5 6 The greater prevalence of severe CAC in HeFH is in accord with the high and early prevalence of clinical CHD in HeFH.7 8

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Table 1: Age distribution of coronary artery calcification in 471 women asymptomatic for coronary heart disease

| Age (years) | <40 | 40–49 | 50–59 | 60–69 | >70 |
|------------|-----|-------|-------|-------|-----|
| n          | 54  | 135   | 155   | 85    | 42  |
| 25%        | 0   | 0     | 0     | 1     | 1   |
| 50%        | 0   | 0     | 5     | 76    |     |
| 75%        | 0   | 0     | 31    | 58    | 379 |
| 90%        | 0   | 24    | 168   | 237   | 517 |

Table 2: Clinical and laboratory characteristics of heterozygous familial hypercholesterolaemia (FH) and normal women

|                     | FH women | Normal women | p Value |
|---------------------|----------|--------------|---------|
| n                   | 27       | 71           | –       |
| Age (years)         | 40 (18)  | 47 (8)       | 0.01    |
| High blood pressure (%) | 14.8   | 11.3         | ns      |
| Smokers and former smokers (%) | 14.8   | 40.8         | 0.017   |
| Obesity (%)         | 14.8     | 12.7         | ns      |
| Diabetes (%)        | 0        | 1.4          | ns      |
| Total cholesterol (mmol/l) | 9.64 (3.91) | 4.95 (0.9) | < 0.0001 |
| HDL-C (mmol/l)      | 7.62 (3.82) | 2.97 (0.74) | < 0.0001 |
| VLDL-C (mmol/l)     | 1.34 (0.25) | 1.47 (0.33) | ns      |
| Triglycerides (mmol/l) | 0.27 (0.1) | 0.22 (0.01) | 0.03    |

Data for age and cholesterol concentrations presented as mean (SD). HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol.
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IMAGES IN CARDIOLOGY

Pulmonary atresia with intact ventricular septum and right coronary artery to right ventricle fistula detected in utero

Pulmonary atresia with intact ventricular septum was diagnosed in a fetus at 29 weeks’ gestation. In addition an enlarged right coronary artery with a fistulous connection to the right ventricle (centre panel). Postnatal ultrasonography (right upper panel) and selective coronary angiography (right lower panel) confirmed the diagnosis.

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