Abstract title: Risk of cardiovascular disease outcomes in primary care subjects with familial hypercholesterolaemia: a cohort study

Iyen, B[1], Qureshi, N[1], Kai, J[1], Akyea, R.K[1], Leonardi-Bee, J[2], Roderick, P[3], Humphries, S.E*[4], Weng,S[1]

[1] Primary Care Stratified Medicine group, Division of Primary care, University of Nottingham, UK
[2] Division of Epidemiology and Public Health, University of Nottingham, UK
[3] Faculty of Medicine, Primary Care and Population Sciences, University of Southampton, UK
[4] Cardiovascular Genetics, Institute of Cardiovascular Science, University College London, UK

Abstract

Introduction: Familial hypercholesterolaemia (FH) is a known major cause of premature heart disease. The risks of atherosclerotic disease in other vascular regions are less known. We determined the risk of major cardiovascular disease (CVD) outcomes associated with clinical FH.

Methods: In a retrospective cohort study (1 January 1999 to 22 July 2016), we randomly-matched 14,097 UK subjects with clinical FH diagnoses or characteristics (Simon-Broome definite (SB) or Dutch Lipid Clinic Network (DLCN) Score >8) to 42,506 subjects without FH by age, sex, general practice. We excluded those with CVD at baseline. Incident rates of coronary heart disease (CHD), stroke or transient ischaemic attack (TIA) and peripheral vascular disease (PVD) were estimated over a median 13.8 years follow-up. Cox proportional hazards regression models stratified on matched-pairs, determined adjusted hazards ratios (HR) for incident CVD in FH compared to non-FH subjects.

Results: The incidence rates (95% CI) of CVD in FH and non-FH subjects (per 1000 person-years at risk) were 25.6 (95% CI 24.8-26.3) and 2.9 (95% CI 2.8-3.1) respectively. The risk of CHD, stroke/TIA and PVD were higher in FH compared to non-FH subjects: CHD (HR 10.63, 95% CI 9.82-11.49), stroke/TIA (HR 6.74, 95% CI 5.84-7.77), PVD (HR 7.17, 95% CI 6.08-8.46). At baseline, 19% of the patients with FH were on lipid- lowering treatment with only 3.2% on high-intensity statins. Over the duration of follow-up, 75% of these subjects with FH had been commenced on lipid-lowering treatment with 38% on high intensity statins. A higher proportion of subjects with FH diagnosis were on lipid-lowering treatment compared to undiagnosed subjects with FH characteristics (SB/DLC phenotype for definite FH). Diagnosed FH subjects had a two-fold higher risk of CHD than subjects without FH. Subjects with undiagnosed FH but the clinical phenotype, had a 15-fold higher risk of CHD as well as statistically higher risk of stroke/TIA and PVD

Conclusions: In addition to the recognised increased risk of CHD, subjects with FH have greatly elevated risk of stroke/TIA and PVD. The risk of stroke/TIA and PVD is particularly higher in undiagnosed subjects with the FH phenotype. This emphasises the importance of early diagnosis and preventive interventions to reduce overall CVD risk in these individuals.