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ORIGINAL ARTICLE

Can Patients be Accurately Assessed for Familial Hypercholesterolaemia in Primary Care?

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Objective Familial Hypercholesterolaemia (FH) is the most prevalent monogenic condition causing premature coronary artery disease, although the majority of individuals remain undiagnosed. We sought to investigate whether individuals with FH could be accurately identified in primary care.

Methods The Dutch Lipid Clinic Network Criteria scores (DLCNCS) assessed by general practitioners (GPs) were compared with DLCNCS assessed by specialists using primary care data in 153 individuals. Thirty individuals with DLCNCS ≥4 underwent specialist review and genetic testing. Clinical FH was defined as DLCNCS ≥6, encompassing the probable and definite FH categories.

Results GPs correctly classified 39 (86.7%) individuals with 'clinical FH', and 32 (94%) with 'unlikely FH' relative to specialists. Lin's concordance correlation coefficient was high (0.832 (0.783 - 0.881), p< 0.001) between specialist and GPs, with an overall agreement of 83.6%, κ 0.744 (0.642 – 0.831). After specialist review, 15 individuals (50%) were diagnosed with clinical FH, four (26.7%) had FH mutations. GPs correctly classified 12 (80%) of these individuals with clinical FH.

Conclusion GPs can accurately identify individuals at high and low risk of FH using the DLCNCS, which may augment opportunistic FH detection in the community. Increased education may enhance the diagnostic accuracy of FH in primary care.

Keywords Familial Hypercholesterolaemia • Primary care • Diagnostic accuracy • Screening • Preventative cardiology

Introduction

Familial hypercholesterolaemia (FH) is an autosomal co-dominant condition characterised by elevated low density lipoprotein cholesterol (LDL-cholesterol), tendon xanthomata and premature coronary heart disease (CHD). The majority of individuals with FH are currently undiagnosed worldwide, with only 1% of the 45,000 people predicted to have FH in Australia being diagnosed [1,2]. FH fulfils the World Health Organization's screening criteria [3], although most countries (including Australia) do not have systematic FH screening programs [1,4].

General practitioners (GP) may be able to assist with FH detection and management in the community [5]. The Dutch

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Lipid Clinic Network Criteria (DLCNC) are the preferred diagnostic criteria for FH in Australia [1,6]. We sought to determine whether GPs could accurately establish the likelihood of FH with the DLCNC.

Methods

Assessment in primary care was carried out by one of three primary care nurses and one of two general practitioners in a rural primary care setting in Western Australia. The nurses were provided with education on calculating the DLCNC score (DLCNCS) at the regional specialist lipid clinic. Individuals at risk of FH were identified by either the laboratory highlighting individuals with elevated LDL-c, or by using an informatics tool to search general practice databases. This occurred as part of a research project that sought to determine the best methods of detecting FH in the community. A nurse would interview and examine all individuals at risk enrolled in the research project and collate the data required for calculating the DLCNCS. If the nurses were unsure if corneal arcus was present, they took photographs of the individual's eyes, which were then de-identified and available as part of the primary care data.

One of the GPs would review the data and calculate the DLCNCS. Then one of the two lipid specialists was provided with the same de-identified data and calculated their own DLCNCS. The lipid specialist remained blind to the GP's DLCNCS. The DLCNCS were preferably calculated using a documented LDL-c off lipid lowering treatment. Although, if an off-treatment LDL-c was unavailable the pre-treatment LDL-c was estimated by adding 30% to the LDL-c obtained while on lipid lowering therapy [7].

The lipid specialist subsequently reviewed 30 individuals (DLCNCS ≥ 4 as assessed by the lipid specialist with primary care data) in a telehealth clinic and determined their likelihood of FH using information obtained during this consultation. The lipid specialist was blind to all previous DLCNCS and the results of FH genetic testing for these individuals, until they had calculated the DLCNCS for the telehealth consultation. Clinical FH was defined as probable or definite FH using the DLCNC categories.

Total cholesterol, triglyceride and high density lipoprotein (HDL)-cholesterol analyses were performed with enzymatic, colorimetric assays using either Abbott, Siemen's or Roche analysers and reagents, depending on the community laboratory the patient presented to. All laboratories were nationally certified. LDL-c was calculated according to the Friedewald equation [8]. Genetic testing was performed as part of routine care, as previously described [9].

Statistical analysis was performed with STATA, StataCorp. 2011, Stata Statistical Software. Agreement on the DLCNCS was assessed using Lin's concordance correlation coefficient, presented with 95% confidence intervals. The agreement between the GPs and specialist's FH likelihood categories based on the DLCNC was assessed using Cohen's kappa

Table 1 Demographic and clinical characteristics of the 153 individuals identified in primary care, and the 30 individuals who underwent specialist review.

	n	153 individuals identified at risk of FH from the community	n	30 individuals with DLCNC $\geq$4 who underwent specialist review
Age years	153	54 (9)	30	54 (9.5)
Male	153	80 (53%)	30	19 (63%)
Total Cholesterol (mmol/L)	109	7.5 (1.7)	23	8.4 (1.7)
LDL-c (mmol/L)	95	5.1 (1.1)	16	6.0 (1.1)
Triglyceride (mmol/L)	97	1.7 (1.3)	16	1.9 (1.0)
HDL-c (mmol/L)	95	1.4 (0.3)	16	1.2 (0.4)
Premature CVD	153	21 (14%)	30	8 (27%)
Premature other vascular disease	153	9 (6%)	30	1 (3%)
FHx prem CVD	153	72 (47%)	30	19 (63%)
FHx elevated cholesterol	153	93 (61%)	30	2 (7%)
Tendon xanthoma	153	3 (2%)	30	0
Corneal arcus	153	11 (7%)	30	5 (17%)
Diabetes	130	15 (11%)	30	5 (17%)
Statin	130	93 (72%)	30	29 (97%)
DLCNC score range with (primary care data)	153	0-12	30	4-11

Continuous variables are expressed as mean and standard deviation. Categorical variables expressed as absolute number and percentage in brackets. N for lipid results is for the number of individuals with documented pre-treatment results. Data for the 153 individuals was from primary care; data for the 30 high risk (DLCNCs ≥ 4) was from the specialist review.