Finding Familial Hypercholesterolaemia After The Event

Calvin MacKinnon[1], William Simpson[2], Rita Patel[3]

[1]Chemical Pathology, Aberdeen Royal Infirmary / General Practice, NHS Grampian,
[2]Department of Clinical Biochemistry, Aberdeen Royal Infirmary and The University of Aberdeen,
[3]Departments of Cardiology / Endocrinology and Diabetes Mellitus, Aberdeen Royal Infirmary

Background

In Familial Hypercholesterolaemia (FH), the exposure to raised LDL-c is lifelong, and consequently, can result in myocardial infarction (MI) at a very young age. If untreated, the incidence of MI in FH has been reported to be about 50% of men by the age of 50 and 50% of women by the age of 60.[1]

NICE guidelines on the condition recommend suspecting a diagnosis of FH in those with total cholesterol >7.5mmol/L or with a personal or family history of premature CHD.[2]

We proposed to assess how frequently FH was being considered as a diagnosis for individuals under the age of 60 hospitalised and diagnosed with myocardial infarction.

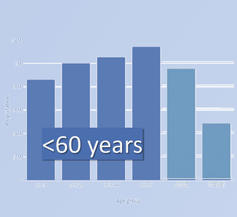
Methods

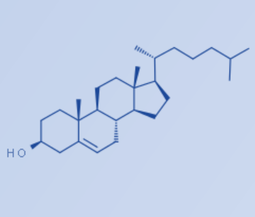
With Caldicott Guardian approval, a retrospective audit was conducted of patients under the age of 60 who were diagnosed as having myocardial infarction in the NHS Grampian regional health board during the 3-year period from 2017 to 2020.

Data for admission episodes of patients coded with ICD-10 code I21 (Acute Myocardial Infarction) were provided by the NHS Grampian Health Intelligence Team.

Lipid criteria for consideration of FH diagnosis were defined as being total cholesterol >7.5mmol/L and/or LDL-c >4.9mmol/L. Potential secondary causes of dyslipidaemia were defined as one of the following: diagnosis of diabetes, diagnosis of hypothyroidism, LFTs > upper limit of normal, and/or a blood alcohol level >100mg/dL.







n	5,500,000	600,000	2855	757	148	92	1
FH*	22,000	2,400	50	30	25	16	16

*estimated prevalence of FH in each group, based on assumed 1/250 population, 5x greater likelihood of MI than population overall[3], 10x greater in <60yrs, most FH with typical LDL, but some complicated by 2y factors

Results

During the study period 2017-2020 NHS Grampian diagnosed 3044 MI in 2855 individuals. The first event for each individual was evaluated.

At the time of first events, 757 were aged <60. Only 344/757 had had lipids checked on admission, but 729/757 had had lipids checked at some point, and 148/729 met lipid criteria for consideration of diagnosis of FH.

Of these 148, 56 could be explained by secondary causes (44 DM, 10 LFT, 6 ETOH, 4 TFT), leaving 92 out of the 757 patients (12.2%) meeting the criteria for consideration of diagnosis of FH.

Genetic testing had been performed in 14 patients, 4 (including 1 FH) known prior to the event, and 10 (including 1 variant of unknown clinical significance) performed after the event. Six individuals were previously known to the lipid clinic (including the FH and 3 others FH tested) and 8 had been referred since the event (including 3 FH tested).

In total, 21 of the 92 patients who met criteria (28.3%) were deemed to have been considered for FH (defined as being either FH tested or referred onward to the lipid clinic for further assessment).

Discussion

It is thought that the prevalence of FH in the UK population is around 1 in 250, but that only 7% of affected individuals have been identified and are known to health services.[4]

In those who have been hospitalised with premature acute coronary syndromes, studies have shown that 14% meet the Simon Broome criteria for possible FH.[5]

Our audit found a similar result at 12.2% but, whereas we would expect an actual prevalence of around 7%, we found a confirmed diagnosis of FH in less than 1% of those who presented with premature MI.

This is far lower than even the estimated population prevalence, which would translate to 3 cases in this sample size, but it has been suggested that individuals with untreated FH have a lifetime risk of CHD approximately 5 times that of the general population, 10 times the risk in those under 60 [3], so we would have expected to find considerably more people with FH in this study population.

Importantly, no new cases of FH were found in any of the patients that were subject to FH gene testing after the event

Conclusion

It is likely that FH is being underdiagnosed not only within the general population but, surprisingly, particularly within those who have experienced premature myocardial infarction. Offering genetic screening routinely to all of these individuals would help to find those individuals who may then benefit from newer treatments, and cascade to their families where prevention could be effective.

References

1. Slack J. Risks of ischaemic heart-disease in familial hyperlipoproteinaemic states. Lancet 1969;2:1380-2
2. National Institute for Health and Care Excellence. Familial hypercholesterolaemia: identification and management [Internet]. [London]: NICE; 2008 [updated 2019 Oct; cited 2021 Aug 21]. (Clinical guideline [CG71]). Available from: https://www.nice.org.uk/guidance/cg71
3. Mundal LJ, Igland J, Veierød MB, et al. Impact of age on excess risk of coronary heart disease in patients with familial hypercholesterolaemia. Heart 2018;104:1600–1607.
4. Akioyamen LE, Genest J, Shan SD, et al. Estimating the prevalence of heterozygous familial hypercholesterolaemia: a systematic review and meta-analysis. BMJ Open 2017;7:e016461
5. Nanchen D, Gencer B, Auer R, Räber L, Stefanini GG, Klingenberg R, Schmied CM, Cornuz J, Muller O, Vogt P, Jüni P, Matter CM, Windecker S, Lüscher TF, Mach F, Rodondi N. Prevalence and management of familial hypercholesterolaemia in patients with acute coronary syndromes. Eur Heart J. 2015 Sep 21;36(36):2438-45.