Canadian Journal of Cardiology 33 (2017) 298–299

Editorial

Familial Hypercholesterolemia: Awareness, Appraisal, and Action

Jacques Genest, MD

Research Institute of the McGill University Health Center, Montréal, Québec, Canada

See article by Brunham et al., pages 385–392 of this issue.

Familial hypercholesterolemia (FH) is the most common monogenic disorder, with a prevalence of approximately 1 in 250 population.[1,2] This would give an estimate of 140,000 cases in Canada. The clinical features of FH rely on an elevated low-density lipoprotein cholesterol (LDL-C) level, a family history of elevated LDL-C, premature atherosclerotic cardiovascular disease (ASCVD), the presence of xanthomas on the extensor tendons, xanthelasmas and premature corneal arcus, and the presence of a mutation in the genes that cause FH (*LDLR*, *APOB,* and *PCSK9*).

Awareness

Yet, physician awareness of this condition is poor, because only a minority of patients are recognized and adequately treated.[3] There are several reasons for this. The clinical features of FH are uncommon; a family history of an elevated LDL-C is difficult to elicit, especially of a parent who is treated with a statin drug; and a family history of premature ASCVD may likewise be difficult to obtain. The diagnostic criteria for FH rely on the Dutch Lipid Clinics Network or the Simon Broome criteria,[4] which might have been taught in medical school but were quickly forgotten and never to be used again (except for the rare lipidologist).

Yet, the experience in the Netherlands shows that FH can be recognized and treated, and targeted screening enables the identification of new cases.[5] This led to 1 of the most extraordinary yet unheralded successes in contemporary medicine. The "natural course" of untreated FH (before effective lipid-lowering therapies) was one of premature ASCVD and death, occurring in the fourth decade of life in men, and 10 years later in women. In the statin drug era, life expectancy is normal if recognition and appropriate treatment is initiated in childhood or early adulthood.[3] To achieve this remarkable result, the Netherlands instituted a registry of patients with FH and put in place health systems to promote the identification of patients, obtain family histories, and enable cascade screening (testing all first-degree relatives). Based on these results, Spain, France, the United Kingdom, and many other countries have followed suit. The US FH Foundation is but the latest example and a global call to arms is meant to raise awareness about FH.[6]

Appraisal

How do we appraise our work with patients who have FH? The article by Brunham et al.[7] examines results from the University of British Columbia (UBC) registry on FH.[7] The registry was initiated just 4 years ago under the leadership of the senior author.[8] This follows similar initiatives in Europe and elsewhere, adapting lessons learned from the experience of the Dutch Lipid Clinics Network.[3] The leaders of the UBC FH registry should be congratulated for examining their data objectively and using metrics as performance indicators.

The Healthy Heart Program at St. Paul's Hospital in Vancouver, British Columbia, Canada is a renowned clinical and research centre staffed with expert clinicians, scientists, and health outcomes researchers. For the present study, they used a strict definition of FH, based on the widely accepted Dutch Lipid Clinic criteria.[4] The demographic data presented are well in keeping with a diverse population. The results presented are important. Despite achieving a high rate of statin drug use in adult patients, only half were receiving a high-potency statin drug. Although many were also receiving ezetimibe, 15% were receiving no treatment and 6.8% were receiving "other lipid-lowering therapies."

This led to an overall average 33% decrease in LDL-C levels from baseline—an encouraging result but still not quite matching the recommended goals of a 50% reduction for primary prevention and < 2.0 mmol/L for secondary prevention.[4,9] Figure 2B in Brunham et al.'s study shows a subgroup analysis of patients achieving a 50% reduction in LDL-C levels.[7] Strikingly, the group of patients with established ASCVD fared less well than patients without this condition. Not unexpectedly, the proportion of patients achieving a LDL-C level < 1.8 mmol/L was very low.

The Kaplan-Meier curves provide some insight into 3700 patient-years of follow-up and show the high rate of

Received for publication September 4, 2016. Accepted September 12, 2016.

Corresponding author: Dr Jacques Genest, Research Institute of the McGill University Health Centre, 1001 Decarie, Montreal, Quebec H4A 3J1, Canada. Tel.: +1-514-934-1934.

E-mail: jacques.genest@mcgill.ca

See page 299 for disclosure information.

http://dx.doi.org/10.1016/j.cjca.2016.09.011

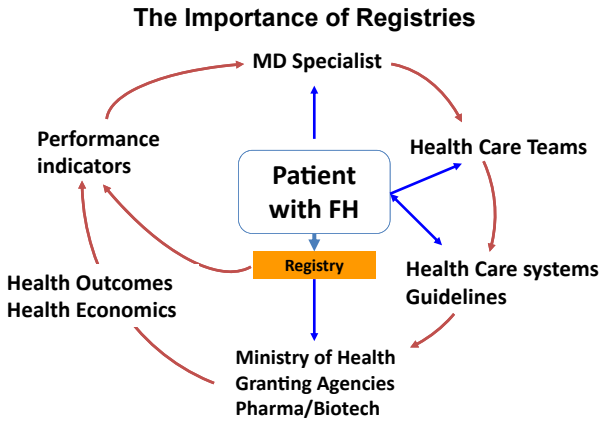

Figure 1. The FH Canada Registry gathers data from individual clinics across Canada to improve patient care and clinical outcomes. Performance indicators are fed back to clinicians and clinics, prompting adjustments in patient care. FH, familial hypercholesterolemia; MD, medical doctor.

cardiovascular events and recurrent cardiovascular events in this population. Not unexpectedly, men with definite heterozygous FH and cardiovascular risk factors fared worse. Spurred by the BC FH registry, a national initiative, FH Canada was created to address the issues of raising awareness, identifying patients, encouraging cascade screening, and offering treatment and novel medications (http://www.FHCanada.net).[10]

The challenge is to meet these goals; the opportunity is to use these data to improve patient care and access to effective therapies and ultimately improve clinical outcomes. The importance of registries in medicine cannot be overemphasized.[11] With the patient at the centre of a continuum of a feedback loop, a patient-centred, disease-specific registry has been shown to influence outcomes in patients with acute coronary syndromes and other forms of cardiovascular diseases (Fig. 1).

Action

As shown by the UBC FH registry, a dedicated group of physicians can champion the care of patients, involve a healthcare team (nurses, dieticians, coordinators) and establish a health service for the province. This initiative has now been taken to a national level. The FH Canada registry was initiated in 2015 and consists of a secure database that is compliant with the Personal Information Protection and Electronic Documents Act.[12] It allows data entry from physicians' offices or clinics or from existing databases. Clinic physicians retain all information concerning their patients, and the anonymized registry data can then be used by researchers and health agencies from the Ministry of Health to determine the burden of disease, health outcomes, and health economics. The simple metrics used in the study by Burnham et al.,[7] namely, absolute LDL-C levels, percentage of LDL-C reduction, and percentage at a specific target, can be used to improve patient care. These data can be fed back to clinicians in the form of publications, clinic audits, and conferences to spur a personalized approach to improve treatment according to current guidelines and improve outcomes.

Funding Sources

FH Canada is supported by unrestricted grants from Amgen, Sanofi, Pfizer, Aegerion, Lilly and Valeant.

Disclosures

Jacques Genest is Co-Chair of FH Canada (www.FHCanada.net).

References

1. De Ferranti SD, Rodday AM, Mendelson MM, et al. Prevalence of familial hypercholesterolemia in the 1999 to 2012 United States National Health and Nutrition Examination Surveys (NHANES). Circulation 2016;133:1067-72.
2. Benn M, Watts GF, Tybjærg-Hansen A, Nordestgaard BG. Mutations causative of familial hypercholesterolaemia: screening of 98 098 individuals from the Copenhagen General Population Study estimated a prevalence of 1 in 217. Eur Heart J 2016;37:1384-94.
3. Nordestgaard BG, Chapman MJ, Humphries SE, et al. European Atherosclerosis Society Consensus Panel. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. Eur Heart J 2013;34:3478-9.
4. Primary Panel Genest J, Hegele RA, Bergeron J, et al. Canadian Cardiovascular Society position statement on familial hypercholesterolemia. Can J Cardiol 2014;30:1471-81.
5. Umans-Eckenhausen MA, Defesche JC, Sijbrands EJ, et al. Review of first 5 years of screening for familial hypercholesterolaemia in the Netherlands. Lancet 2001;357(9251):165-8.
6. Vallejo-Vaz AJ, Kondapally Seshasai SR, Cole D, et al. Familial hypercholesterolaemia: a global call to arms. Atherosclerosis 2015;243:257-9.
7. Brunham LR, Cernmakova L, Lee T, et al. Contemporary trends in the management and outcomes of patients with familial hypercholesterolemia in Canada: results from a prospective observational study. Can J Cardiol 2017;33:385-92.
8. Al-Sarraf A, Allard M, Martinka M, Frohlich J. Regional and national familial hypercholesterolemia registries: present international application, importance, and needs for Canada. Can J Cardiol 2013;29:6-9.
9. Anderson TJ, Gregoire J, Pearson GJ, et al. 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. Can J Cardiol 2016;32:1263-82.
10. FH Canada. Available at: http://www.fhcanada.net. Accessed September 9, 2016.
11. Roe MT, Messenger JC, Weintraub WS, et al. Treatments, trends, and outcomes of acute myocardial infarction and percutaneous coronary intervention. J Am Coll Cardiol 2010;56:254-63.
12. Office of the Privacy Commissioner of Canada. The Personal Information Protection and Electronic Documents Act (PIPEDA). Available at: https://www.priv.gc.ca/leg_c/leg_c_p_e.asp. Accessed August 21, 2016.