Familial Hypercholesterolemia Patients Response to a Free Genetic Testing Offer

Samuel S. Gidding MD[1], Amanda Sheldon[1], Sherman Law[2], Cynthia L. Neben PhD[2], Hannah E. Williams MPH[2], Alicia Y. Zhou PhD[2], Katherine Wilemon[1], Catherine Davis Ahmed[1], Iris Kindt MD, MPH[1]

[1]The FH Foundation, Pasadena CA, [2]Color Genomics, Burlingame CA

Background

In the United States, cascade screening for familial hypercholesterolemia (FH) is recognized as a Tier 1 genomic application by the Centers for Disease Control and Prevention, meaning that performance of cascade screening for FH is clinically important, similar to Lynch syndrome and Hereditary Breast and Ovarian Cancer Syndrome (HBOC). Nonetheless, in the United States, genetic testing for FH is performed infrequently. In the FH Foundation CASCADE FH® Registry, only 8% have undergone genetic testing, compared to over 90% in most registries around the world where genetic testing for FH is routinely performed.

Barriers to genetic testing in the United States include cost, patient interest, patient concerns about the implications of testing for future care, genetic discrimination, need for a physician order, and under-utilization of genetic counseling in the testing process.

The purpose of the FH Foundation's PAGENT (Patient Acceptance of GENetic Testing) study was to determine the spontaneous uptake of genetic testing, with some of these barriers removed. Phenotypically diagnosed FH participants in the Patient Portal of the FH Foundation CASCADE FH Registry were studied. Free genetic testing was offered to clinically diagnosed FH patients through the Patient Portal; uptake of the genetic testing offer and yield from cascade genetic testing on those with positive genetic tests were study outcomes.

Objectives

- To describe the yield from an offer for free FH genetic testing from a clinically diagnosed FH cohort (no prior genetic testing).
- To describe the yield from cascade testing of those testing positive.

Methods

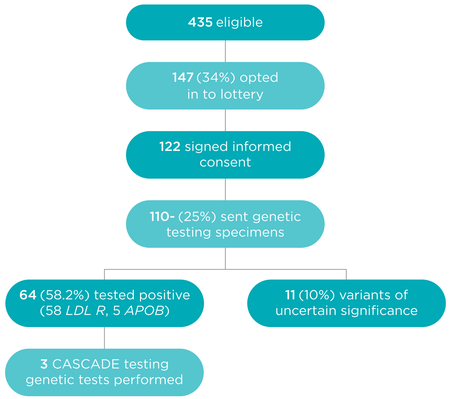
- Cohort assembled from the Patient Portal of the CASCADE FH Registry.
- Participants were asked if they wanted to receive free genetic testing for FH.
- Those providing informed consent were sent genetic testing kits.
- Genetic testing for variants in LDL-R, APOB, and PCSK9 performed at Color Genomics.
- If positive for an FH variant, participants received genetic counseling from a Color Genomic genetics counsellor and were asked to identify eligible family members for free CASCADE testing.
- Yield at each step in the process and demographic data were collected.

Genetic Testing

Laboratory procedures were performed at the Color laboratory under CLIA and CAP compliance. Briefly, DNA was extracted, enriched for select regions using SureSelect XT probes, and then sequenced using NextSeq 500/550 or NovaSeq 6000 instrument. Sequence reads were aligned against human genome reference GRCh37.p12. Variants are identified using a suite of bioinformatic tools designed to detect single nucleotide variants, small insertions and deletions (indels, 2-50 bp), and large structural variants (> 50 bp).

Variants were classified according to the American College of Medical Genetics and Genomics 2015 guidelines for sequence variant interpretation, and all variant classifications were signed out by a board-certified medical geneticist or pathologist.

Results



Presence of a positive family history (87% vs. 32%) or LDL-cholesterol > 250 mg/dL was associated with having a positive genetic test

Comparison of self-reported characteristics among FH patients with a positive (n=64) and negative (n=46) genetic test results

Results Summary

- About 25% of those asked to participate obtained free genetic testing.
- Yield for cascade screening poor.

Limitations

- Demographics and health history information were self-reported.
- Difficult to comment on why participants were lost to follow-up as we did not have systematic data collection for those who dropped out after each phase of the study.
- The study did not survey patients who were offered free genetic testing to ascertain why they did or did not participate, or how they experienced genetic test results, positive, negative, or VUS.

Conclusions

- Free genetic testing is an incentive for patient participation in the genetic testing process for FH but barriers still exist for CASCADE screening.
- Healthcare providers should be prepared to counsel FH patients who undergo genetic testing and receive negative results and/or a variant of uncertain significance.

Conflicts of Interest

SG, AMS, KW, and CDA are employees/officers of the FH Foundation, a 501c3 advocacy and research organization dedicated to improving care for those with familial hypercholesterolemia.

IK was an employee of the FH Foundation at the time of data collection for the study.

SL, CN, HEW and AYZ have equity interest in and are employed by Color Genomics.

Contact

The FH Foundation
959 E. Walnut Street Suite 220
Pasadena, CA 91106
(626) 583-4674
FHregistry@thefhfoundation.org