Ambry Genetics

RESEARCH FOR YOUR PRACTICE

Ambry's Multigene Panel Testing Finds Families with Unexpected *CDH1* Mutations

HOW DO WE BEST MANAGE THESE FAMILIES? AMBRY HELPS FIND THE ANSWER.

A recent collaboration between Ambry Genetics, University of Southern California, and Stanford University published in JCO Precision Oncology[1] describes the incidence and clinical characteristics of *CDH1* mutation carriers found through multigene panel testing (MGPT).

WHY THIS MATTERS TO YOU

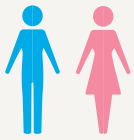
Some patients found to have a *CDH1* mutation via MGPT do not meet clinical criteria for hereditary diffuse gastric cancer (HDGC), posing a management challenge. We studied different families with a *CDH1* mutation and offered management recommendations.

BACKGROUND

HDGC is a rare condition caused by *CDH1* mutations, and associated with up to an 80% lifetime risk of diffuse gastric cancer (DGC) and up to a 60% lifetime risk for female invasive lobular breast cancer (ILC), therefore needing increased breast cancer screening and to consider prophylactic gastrectomy.[2]

Providers are increasingly ordering MGPT, which often includes *CDH1,* resulting in the identification of unexpected mutations in patients who do not meet the International Gastric Cancer Linkage Consortium (IGCLC) criteria.[3,4] Given the serious nature of a gastrectomy, providers question whether these patients should be treated with the same surgical measures used for those with classic HDGC.

This study assessed the clinical histories of 20 *CDH1* mutation carriers identified by MGPT (out of 27,254 tested) to determine if they met IGCLC criteria and offer informed recommendations for medical management.



20 patients identified to have a *CDH1* mutation by MGPT

POINTS FOR YOUR PRACTICE

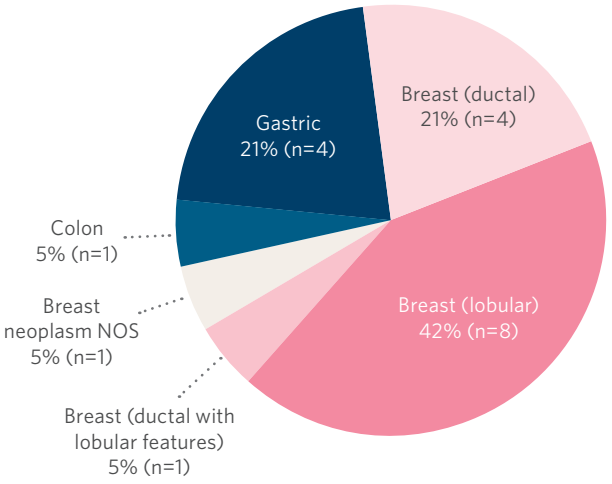
- IGCLC criteria may miss patients with *CDH1* mutations; however, MGPT may help to identify these families
- Ambry includes analysis of *CDH1* on several panels, including BreastNext, ColoNext, and CancerNext
- Many healthcare providers, including expert authors on this study, continue to manage all *CDH1* mutation carriers according to current guidelines, with consideration of prophylactic gastrectomy between 20-30y and annual breast MRI beginning at 30y.[3,4]

"These guidelines may change as we gain additional knowledge on the cancer risks, and until then, counseling and support balanced by consideration of risks, benefits and costs are integral to partnering with these patients in shared decision-making."[1] - Study Author

SIGNIFICANT FINDINGS

- Breast cancer was the most prevalent cancer, present in 73% of mutation carriers
  - 21% of mutation carriers had ductal breast cancer, not the typical lobular breast cancer associated with *CDH1* mutations
- 65% of patients **did not meet** IGCLC criteria for consideration of *CDH1* testing
- 3 patients had prophylactic gastrectomy, and all had pathologic evidence of DGC, despite not meeting IGCLC criteria, highlighting the importance of a well-informed management plan

Cancer Types in *CDH1* Mutation Carriers



Learn more about our research here.

REFERENCES

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