

Hereditary Diffuse Gastric Cancer (HDGC) - *CDH1* Mutations

What You Should Know About *CDH1* Mutations/Hereditary Diffuse Gastric Cancer

Individuals with a *CDH1* mutation have a condition called Hereditary Diffuse Gastric Cancer (HDGC). HDGC accounts for less than 1-3% of all gastric cancer. Diffuse Gastric cancer is a specific type of invasive stomach cancer that thickens the wall of the stomach wall without forming a distinct tumor. Diffuse gastric cancer is also called signet ring carcinoma or isolated cell-type carcinoma. Women with HDGC are at significantly increased risk to develop lobular breast cancer. Certain other types of breast cancer, as well as colon cancer and pancreatic cancer have been reported in patients with HDGC.

Cancer Risks Associated with a *CDH1* Mutation

It is estimated that the lifetime risk for gastric cancer for men with HDGC is 67-70% and 56-83% for women. The majority of patients develop diffuse gastric cancer by the age of 40. Women with HDGC have a 39-52% lifetime risk of developing lobular breast cancer. The average age of onset 53 years.

Risks to Family Members

Mutations in the *CDH1* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *CDH1* mutation have a 1 in 2 (50%) chance of having the mutation as well. Individuals with a *CDH1* mutation may develop *CDH1* cancer, or none of the above. Both males and females can inherit a familial *CDH1* mutation and can pass that it on to their children.

Managing Cancer Risks

Once an individual has been diagnosed with HDGC, endoscopies should be done annually, but usually not for patients younger than age 16. An endoscopy involves inserting a camera on the end of a tube down a patient's throat into their stomach. Usually beginning at 35 years of age, females should have annual mammograms and breast MRIs, as well as biannual clinical breast exams, to evaluate for breast cancer.

Evidence suggests removal of the stomach (gastrectomy) is significantly better at preventing diffuse gastric cancer than endoscopic surveillance. Gastrectomy is generally not recommended for patients younger than 20 years old. Cancer screening should begin earlier if family members have been diagnosed with cancer at young ages.

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