

Technical and Endoscopic Factors in Gastric Cancer Surveillance in *CDH1* Mutation Carriers

Carol A. Burke^{1,3,5}, Michael Cruise^{2,5}, Lisa LaGuardia^{3,5}, Margaret O'Malley^{3,5}, Matthew Kalady^{3,5}, James Church^{3,5}, Gautam Mankaney^{1,5}, David Liska^{3,5}, Brandie Leach^{4,5}

Departments of Gastroenterology¹, Anatomic Pathology²,
Colorectal Surgery³, Genomic Medical Institute⁴

*Sanford R. Weiss MD Center for Hereditary Colorectal Neoplasia*⁵

Cleveland Clinic, Cleveland, OH



Gastric Cancer Risk Management in *CDH1* mutation carriers

- Cumulative Lifetime Risk of Diffuse Gastric Cancer¹
 - 70% in men
 - 83% in women
- Prophylactic total gastrectomy (TG) recommended between ages of 18-40 years²
- EGD recommended preoperatively
- Annual EGD surveillance if TG not performed³

¹Fitzgerald, J Med Genet 2010;47:436

² Gastric Cancer. NCCN Guidelines v2. 2018

³ Van der Post, J Med Genet 2015;52:361

Cambridge Protocol for EGD

- Perform in center of expertise
- White light, high definition endoscope
- ≥ 30 min inspection
- Clean mucosa with adjunctive agents; evaluate inflated/deflated
- Targeted biopsy of abnormalities including pale areas
- ≥ 5 random biopsies each in pre-pyloric area, antrum, transitional zone, body, fundus and cardia
- *Taking more than 30 biopsies is not feasible in practice*

EGD Detection of Signet Ring Cancer in *CDH1*

Year	No. pts	Population	EGD findings	Protocol for Surveillance	Yield of EGD Bx for SRC
2009 ¹	23	Retrospective, pts s/p prophylactic TG	Normal	Multiple random bx	9%
2011 ²	10	Retrospective, pts s/p prophylactic TG	Gastritis	Not described	10%
2011 ³	13	Series, consecutive asymptomatic patients	Normal	Standard + high mag EGD w/ chromo; >6 random Bx; EUS	15%
2018 ⁴	174	Literature review, asymptomatic pts s/p TG	Lesions in 12%	Not described	28%
2018 ⁵	54	Cohort <i>CDH1</i> patients meeting HDGC criteria	Pale areas in 28%	White light, high resolution EGD (GIF-Q260Z); NBI and autofluorescence imaging of lesions, Targeted & random Bx	61%

¹Hebbard PC, Ann Surg Oncol 2009;16:1890; ²Pandalai PK, Surgery 2011;149:347; ³Chen Y, Ann Surg Oncol 2011;18:2594; ⁴Rocha J, Histopathology 2018;73:878; ⁵Mi E, Gastrointest Endosc 2018;18:408

Weiss Center Practice Today

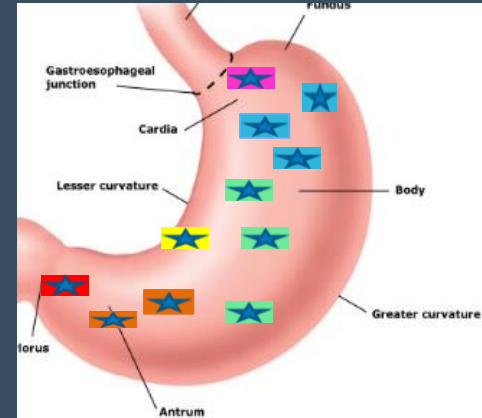
- Rapid rise in *CDH1* mutation carriers
- Due to diagnosis on multi-gene cancer panel testing



AIM

- To describe the endoscopic aspects and pathology findings in *asymptomatic* adults with pathogenic variant in *CDH1* undergoing endoscopic surveillance in our Center

Methods



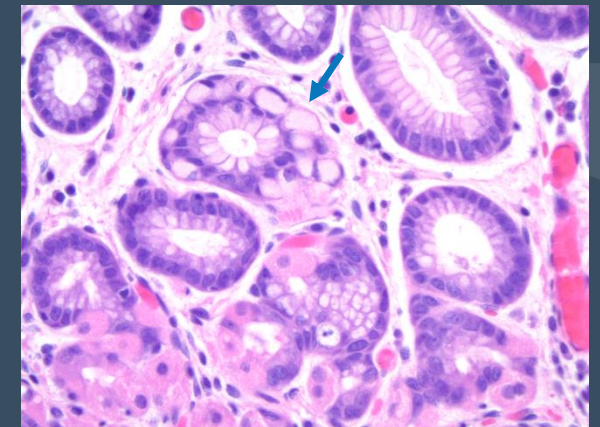
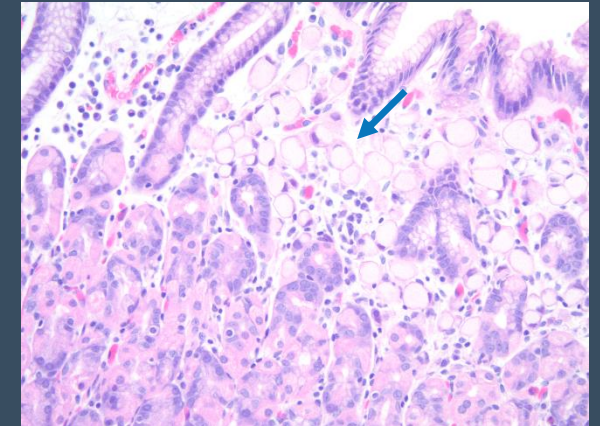
- High definition white light and narrow band imaging endoscopy (Olympus GIF HQ 190)
- Conscious sedation
- Targeted biopsy of lesions
- ≥ 77 random biopsies; 7 each 4 quadrants from **cardia**, **pre-pylorus**, **antrum** (distal, proximal), **transition zone**, **body** (proximal, mid, distal), **fundus** (proximal, mid, distal)
- Surveillance interval 1 year in patients who refuse TG

Results: Patient and EGD related factors

No. patients	18
Age 1 st EGD (range)	46.8 yrs (29-63)
Age last EGD (range)	47.8 years (36-65)
Female gender	11 (61%)
Total number of EGDs	27
1	13 patients (73%)
2	2 patients (11%)
3	2 patients (11%)
4	1 patient (5%)
Average Procedure Length	27.8 mins
Endoscopic Complications	0
No. EGDs /Endoscopist	
Endoscopist: 1	25/27 (93%)
Endoscopist: 2 and 3	2/27 (7%)

Results

Yield of EGD for Signet Ring Cell Cancer Detection	
No. pts with Signet Ring Cell Cancer	9/18 (50%)
Exam when detected by EGD	7/9 (78%)
1 st EGD	5
2 nd EGD	1
3 rd EGD	1
Not detected @ EGD	2 (at prophylactic TG)
Yield on Targeted bx (pale patch/nodule)	5/7 (71.5%)
Yield on Random bx	2/7 (28.5%)
Cancer location in TG specimen	Known in 7/9
Fundus in 7/7	7/7
Fundus and antrum	2/7
Pathology	
T1N0M0	9/9 (100%)



Conclusions

- Utilizing our protocol, we report the highest known rate of signet ring cell cancer detection by EGD
- Diffuse Gastric Cancer most likely found on 1st EGD
 - Located in proximal stomach
 - On targeted biopsy
 - Diagnosed at early stage
- It is feasible and safe to take ≥ 30 biopsies
- Yield of our protocol outside Cleveland Clinic should be assessed



Every life deserves world class care.