Clinicopathologic Characterization and Genotype Correlation of Duodenal Polyposis among Hispanics with Familial Adenomatous Polyposis

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Introduction

- Specialized guidelines have improved prognosis of patients with familial adenomatous polyposis (FAP).
- Patients remain at increased risk for other neoplasia such as duodenal cancer.
- The Spigelman Classification for duodenal polyposis was designed to estimate a patient's risk for duodenal cancer based on endoscopic and histopathologic findings.
- Variations in colonic polyposis following a genotype-phenotype pattern according to APC gene mutation have been documented.
- The genotype-phenotype relationship in duodenal polyposis remains less clear.

Criteria	Points		
	1	2	3
Polyp number	1-4	5-20	>20
Polyp size (mm)	1-4	5-10	>10
Histology	Tubular	Tubulovillous	Villous
Dysplasia	Mild	Moderate	Severe

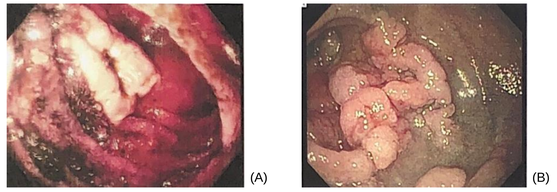
Table 1: Spigelman Classification for duodenal polyposis in FAP (Stage 0 = 0 points; Stage I = 1-4 points; Stage II = 5-6 points; Stage III = 7-8 points; Stage IV = 9-12 points

Specific Aims

- I: To characterize duodenal adenomatosis and ampullary adenomas in FAP in correlation with genotypic, sociodemographic, and epidemiologic factors among Hispanics.
- II: To examine associations between differences in genotype and their impact in the severity of duodenal adenomatosis, as indicated by the Spigelman Classification for duodenal polyposis in FAP.
- III: To determine the lifetime risk of duodenal neoplasia in Hispanic patient with FAP who are receiving long-term endoscopic surveillance.

Methodology

- 71 patients with FAP who had undergone at least one (EGD) with evaluation of the duodenum were included.
- Age, sex, tobacco use, alcohol use, and BMI were among the sociodemographic factors evaluated.
- Study population was divided into mutations in the APC gene between codons 1000-1500 (Group 1) versus mutations before codon 1000 and after codon 1500 (Group 2).
- Participants were recruited from IRB-approved registry (http://purificar.rcm.upr.edu/)



(A) (B)

Figure 1. Flat 15mm polyp in duodenum (A). Multiple broad-based polyps from the medial to lateral aspect of the second part of the duodenum (B).

Results

- Duodenal adenomas were present in 42 (59%) and ampullary adenomas were present in 17 (24%) FAP patients: 15 (21%) had both duodenal and ampullary adenomas.
- 120 EGDs were evaluated for the study, with a mean of 1.7 EGDs per patient (Range = 1 – 4).
- Analysis of established sociodemographic variables showed no independent association with development of duodenal or ampullary adenomas (Table 2).

Table 2: Sociodemographic analysis of patients with adenomas (duodenal and/or ampullary) versus those without, demonstrating no significant statistical differences.

Characteristics	Group		p-value
Sex (n=71)	**Adenoma N=44**	**Control N=27**	
Male	23 (52.3)	17 (63.0)	0.378
Female	21 (47.7)	10 (37.0)	
Age at first endoscopy (n=71)			
Median (min-max)	34 (8-65)	35 (15-69)	0.447
Age at last contact (n=71)			
Median (min-max)	41 (10-71)	37 (19-69)	0.700
BMI (n=69)			
Underweight (<18.5)/Normal weight (18.5-24.9)	22 (52.4)	12 (46.2)	0.618
Overweight (25-29.9)/Obesity (>30)	20 (47.6)	14 (53.8)	
Lifetime smoker (>100 cigarettes) (n=70)			
No	32 (72.7)	20 (80)	0.5
Yes	12 (27.3)	5 (20)	
Alcohol in last 12 months (at interview) (n=58)			
<1 per week	24 (64.9)	11 (52.4)	0.432
>= 1 per week	13 (35.1)	10 (47.6)	

- Patients with duodenal adenomas on EGD were more likely to have APC mutations between codons 1000-1500 (Table 3).
- Differences in Spigelman stage between both genotype groups were not statistically significant (Table 4).
- No cases of duodenal or ampullary cancer were observed after an overall follow-up of 304.6 patient-years.

Table 3: Patients with duodenal adenomas on EGD had significantly greater prevalence of mutations in 1000-1500 cluster of the APC gene.

Characteristics	Group		p-value
	Codons 1000 and 1500 n(%)	Codons <1000 or >1500 n(%)	
Duodenal adenoma (n=35)	23 (65.7)	12 (34.3)	0.001
No duodenal adenoma (n=25)	5 (20.0)	20 (80.0)	

Table 4: No significant statistical correlation between Spigelman Stage and affected region of the APC gene.

Characteristics	Group		p-value
Spigelman Stage (n=20)	Between codons 1000 and 1500	Codons <1000 or >1500	
I	7 (70.0)	3 (30.0)	0.861
II	4 (80.0)	1 (20.0)	
III	3 (100.0)	0 (0.0)	
IV	2 (100.0)	0 (0.0)	

Conclusions

- Our study provides the first phenotypic and genotypic characterization of duodenal polyposis among Hispanic patients with FAP.
- Duodenal polyposis was significantly associated with APC mutations within the 1000-1500 codon cluster (classic FAP).
- No other clinicodemographic or environmental associations were independently associated with presence of duodenal polyposis.
- No cases of duodenal cancer were observed in 304.6 patient-years of follow up.
- Our observations provide insightful information about the impact of APC genetic mutation location and endoscopic surveillance.
- Long-term studies are warranted to evaluate the impact of duodenal neoplasia in patients with FAP.

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