Prevalence of mutations in hamartomatous/mixed polyposis genes in patients with multiple colon polyps stratified by age

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Background: Multiple colorectal polyps are a "red flag" for certain hereditary cancer syndromes. The utility of testing older patients for hamartomatous/mixed polyposis genes is unknown. Our aim was to examine the prevalence of pathogenic mutations in these genes in patients with unselected polyposis stratified by age.

Methods: A cross-sectional study of patients undergoing multigene panel testing at a commercial laboratory was performed. Data was obtained from test requisitions and available records (3/2012 – 12/2016). All patients had 10 or more colorectal polyps of any type and were sorted by age at testing and total polyp count (10-19, 20-99 and 100+). We assessed the prevalence of mutations in *SMAD4*, *BMPR1A*, *PTEN*, *STK11,* and *GREM1*. Chi-square tests and Cochran-Armitage tests were utilized. Groups with less than 10 patients were excluded.

Results: Of the 3,802 patients meeting criteria, mutations were found in 103 patients (2.7%). *PTEN* (32%), *BMPR1A* (28.2%) and *SMAD4* (28.2%) mutations were most common. Mutation prevalence decreased with age in patients with 10-19 and 20-99 polyps (p<0.001 for both), but not in those with 100+ polyps (p=0.69). Patients with 10-19 polyps tested over age 50 and patients with 20-99 polyps tested over age 70 had a mutation prevalence of < 1% (Table).

Conclusions: Prevalence of mutations in hamartomatous/mixed polyposis genes decreased with age in patients with less than 100 polyps but remained high in those with over 100 polyps. Sub-analyses by polyp type will help further refine mutation prevalence and elucidate when testing yield is highest for these genes.

Table. Prevalence of mutations in hamartomatous/mixed polyposis genes.

Age at Testing	N	Total number of colorectal polyps		
		10-19	20-99	100+
10-19	31 (0.8%)	6.7%	*	*
20-29	85 (2.2%)	10.5%	32.4%	10.3%
30-39	216 (5.7%)	5.0%	9.5%	9.4%
40-49	445 (11.7%)	3.3%	6.1%	7.8%
50-59	1111 (29.2%)	0.6%	3.3%	9.4%
60-69	1281 (33.7%)	0.7%	1.4%	2.9%
70-79	543 (14.3%)	0.0%	0.6%	4.8%
80-89	90 (2.4%)	0.0%	0.0%	*

*Indicates n < 10