Prevalence of mutations in adenomatous polyposis and colorectal cancer-associated genes in patients with multiple colon polyps stratified by age

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Background: Current guidelines recommend genetic testing for patients with ≥10 colon adenomas. Data is lacking regarding the utility of testing older patients, as well as using larger multigene panel testing (MGPT). We examined the prevalence of pathogenic mutations in polyposis patients stratified by age.

Methods: A cross-sectional study of patients undergoing MGPT at a commercial laboratory was performed. Data was obtained from test requisitions and available records (3/2012 – 12/2016). All patients had ≥10 colon polyps including adenomas. The cohort was sorted by age at testing and polyp count (10-19, 20-99, ≥100). We assessed the prevalence of mutations in adenomatous polyposis genes (*APC*, biallelic *MUTYH*, *POLE*, *POLD1,* biallelic mismatch repair deficiency) and non-polyposis colorectal cancer genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM, TP53*, *CHEK2*, *CDH1*). Chi-square and Cochran-Armitage tests were utilized. Groups with <10 patients were excluded.

Results: 3,221 patients met inclusion criteria. Mutation prevalence in polyposis genes decreased with age in all polyp count groups ($p < 0.001$). Notably, patients with 10-19 polyps tested over age 60 had mutation prevalence <1% (Table 1). Mutation prevalence in non-polyposis colorectal cancer genes remained high in all age groups and was not associated with age in all polyp count groups ($p = 0.3$ or greater).

Conclusions: Older patients with multiple polyps including adenomas had lower prevalence of mutations in polyposis genes, but maintained a high rate of mutations in other colon cancer-associated genes. We recommend continued genetic testing of these patients regardless of age and would recommend MGPT to include other non-polyposis colorectal cancer genes.

Table 1. Prevalence of mutations in adenomatous polyposis genes.

		Total number of colorectal polyps		
Age at Testing	**N**	**10-19**	**20-99**	**100+**
10-19	21 (0.7%)	10.0%	*	*
20-29	64 (2.0%)	13.3%	28.0%	70.8%
30-39	175 (5.4%)	8.0%	18.9%	57.7%
40-49	380 (11.8%)	6.5%	20.4%	48.8%
50-59	936 (29.1%)	1.8%	10.4%	36.7%
60-69	1096 (34.0%)	0.7%	6.1%	30.4%
70-79	469 (14.6%)	0.7%	2.7%	10.5%
80-89	80 (2.5%)	0.0%	5.0%	*

* Indicates n < 10

Table 2. Prevalence of mutations in non-polyposis colorectal cancer genes.

		Total number of colorectal polyps		
Age at Testing	**N**	**10-19**	**20-99**	**100+**
10-19	21 (0.7%)	0.0%	*	*
20-29	64 (2.0%)	6.7%	0.0%	4.2%
30-39	175 (5.4%)	2.7%	1.4%	3.8%
40-49	380 (11.8%)	4.9%	4.6%	2.3%
50-59	936 (29.1%)	3.7%	2.4%	4.1%
60-69	1096 (34.0%)	4.4%	2.6%	3.6%
70-79	469 (14.6%)	4.6%	3.7%	0.0%
80-89	80 (2.5%)	7.7%	7.5%	*

* Indicates n < 10