RISK FACTORS ASSOCIATED WITH ADENOMA MULTIPICITY IN A SCREENING COHORT

B. Sullivan1,2, D. Abbott2, M. O’Leary2, E. Hauser1,2, C. Williams2, R. McNeil2, L. Musselwhite1,2, D. Weiss3, Z. Gellad1,2, D. Lieberman4, D. Provenzale1,2
1Duke University, Durham, NC 2Cooperative Studies Program Epidemiology Center, Durham Veterans Affairs Medical Center, Durham, NC 3Cooperative Studies Program Coordinating Center, Perry Point Veterans Affairs Medical Center, Perry Point, MD 4Portland Veteran Affairs Medical Center, Portland, OR

Background

Little is known about the prevalence, clinical characteristics, and long-term outcomes of patients with ≥10 cumulative adenomas.

Aims

• Estimate the proportion of individuals undergoing screening colonoscopy who develop ≥10 cumulative adenomas.
• Examine the demographic and baseline clinical risk factors that are associated with having ≥10 cumulative adenomas.
• Describe the proportion of patients with advanced neoplasm (AN) and colorectal cancer (CRC).

Patients and Methods

The Prospective Evaluation of Risk Factors for Large (≥1 cm) Colonic Adenomas in Asymptomatic Subjects (CSP 380) cohort is comprised of 3121 subjects age 50-75 who had a screening colonoscopy between 1994 and 1997. These patients were followed for 10 or more years until death or last colonoscopy. This analysis includes the 3089 subjects with no cancer at baseline. At least one follow-up exam was performed in 1975 patients.

Baseline characteristics of subjects with ≥10 cumulative adenomas were compared to those of subjects with 0-9 cumulative adenomas.
• Demographic and lifestyle factors
• Proportion with AN (defined as polyp ≥1 cm, villous histology, high grade dysplasia, or CRC)

Results

Table 1: Risk Factors Associated with ≥10 or More Cumulative Adenomas

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Number of Patients with ≥10 Adenomas (N=101)</th>
<th>Number of Patients with &lt;10 Adenomas (N=2939)</th>
<th>Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1,090 (89.8%)</td>
<td>1211 (119.5%)</td>
<td>1.74 (1.40 - 2.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male</td>
<td>746 (65.0%)</td>
<td>500 (65.0%)</td>
<td>1.00 (0.40 - 2.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>2,537 (85.1%)</td>
<td>711 (73.7%)</td>
<td>1.19 (1.01 - 1.40)</td>
<td>0.04</td>
</tr>
<tr>
<td>Smoking status</td>
<td>399 (84.9%)</td>
<td>848 (84.9%)</td>
<td>1.19 (0.97 - 1.48)</td>
<td>0.08</td>
</tr>
<tr>
<td>Family History of Colonic Polyps</td>
<td>2,441 (87.9%)</td>
<td>721 (78.9%)</td>
<td>1.00 (0.40 - 2.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>One Degree of Ancestry with CRC</td>
<td>3,200 (89.0%)</td>
<td>1120 (124.9%)</td>
<td>1.40 (1.30 - 1.50)</td>
<td>0.001</td>
</tr>
<tr>
<td>Two Degrees of Ancestry with CRC</td>
<td>1,339 (69.0%)</td>
<td>748 (60.7%)</td>
<td>2.74 (2.19 - 3.46)</td>
<td>0.001</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1,140 (89.8%)</td>
<td>1131 (119.5%)</td>
<td>1.20 (1.02 - 1.42)</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>749 (85.3%)</td>
<td>515 (55.7%)</td>
<td>2.61 (2.20 - 3.11)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Findings

Table 2: Proportion of Patients with AN and CRC

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients with 0-9 Adenomas</th>
<th>Patients with ≥10 Adenomas</th>
<th>Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Colonoscopies</td>
<td>3023 (97.9%)</td>
<td>66 (2.1%)</td>
<td>1.25 (1.00 - 1.56)</td>
<td>0.04</td>
</tr>
<tr>
<td>Average Number of Colonoscopies</td>
<td>3.6</td>
<td>3.9</td>
<td>1.20 (1.02 - 1.42)</td>
<td>0.02</td>
</tr>
<tr>
<td>Days Between Colonoscopies</td>
<td>4576.7</td>
<td>553.7</td>
<td>0.96 (0.80 - 1.23)</td>
<td>0.65</td>
</tr>
<tr>
<td>Finding of AN</td>
<td>348 (11.5%)</td>
<td>42 (63.5%)</td>
<td>6.00 (3.00 - 12.00)</td>
<td>0.001</td>
</tr>
<tr>
<td>Finding of CRC</td>
<td>25 (0.8%)</td>
<td>2 (3.0%)</td>
<td>2.40 (0.60 - 9.60)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

• Ten or more cumulative adenomas were found in 66 (2.1%) of the 3089 patients.
• Patients with ≥10 cumulative adenomas had more frequent colonoscopies with a shorter interval between examinations.
• AN was found in more than half (64%) of these patients, and CRC in 3%.
• Age 60-69 is the single baseline risk factor associated with ≥10 adenomas.
• Subjects with ≥10 cumulative adenomas had a markedly higher risk of AN.
• Two patients with <10 adenomas at baseline developed ≥10 adenomas and subsequent CRC. Their time course, number of colonoscopies, and colonoscopy findings are shown in Figure 1.

Conclusions

• We identified ≥10 cumulative adenomas in about 2% of this screening population, with few cases before age 60.
• There is no identifiable cluster of demographic and clinical risk factors associated with the finding of ≥10 cumulative adenomas.
• Few patients with ≥10 cumulative adenomas go on to develop CRC. Additional factors are needed for more effective risk stratification and identification of those who might benefit from genetic counseling.

Future Work

• Evaluate the proportion and impact of genetic counselling referrals in patients with ≥10 cumulative adenomas.
• Identify potential genomic factors associated with an increased risk of adenoma multiplicity, AN, and CRC, using blood and tissues collected from this cohort.
• Validate these findings in a larger screening cohort.
• Develop a post-baseline colonoscopy risk stratification tool that can identify patients at high risk for an underlying genetic CRC syndrome and likely to develop interval AN or CRC, as these patients are more likely to benefit from continued intensive surveillance and earlier genetic counseling.

Acknowledgments

This research was supported by the VA Cooperative Studies Program (VA CSP) and the Duke University Resident Faculty Research Grant.

References


Figure 1. Surveillance Colonoscopies & Interval Cancer Diagnosis

Future Work

• Evaluate the proportion and impact of genetic counselling referrals in patients with ≥10 cumulative adenomas.
• Identify potential genomic factors associated with an increased risk of adenoma multiplicity, AN, and CRC, using blood and tissues collected from this cohort.
• Validate these findings in a larger screening cohort.
• Develop a post-baseline colonoscopy risk stratification tool that can identify patients at high risk for an underlying genetic CRC syndrome and likely to develop interval AN or CRC, as these patients are more likely to benefit from continued intensive surveillance and earlier genetic counseling.