Association of tobacco and alcohol use with earlier development of colorectal pathology: should screening guidelines be modified to include these risk factors?

Mario Rueda, M.D., Yara Robertson, M.D., Alison Acott, M.D., Steven Rueda, B.S., Aaron Keikhoff, B.S., Whitney Guerrero, B.S., Anne T. Mancino, M.D., F.A.C.S.*

Department of Surgery, Central Arkansas Veterans Healthcare System, 4300 W 7th Street, 112/LR, Little Rock, AR 72205, USA

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Abstract

BACKGROUND: Current guidelines for colorectal cancer (CRC) screening recommend initial screening at 50 years of age for normal-risk patients. Alcohol and tobacco use can be associated with an earlier onset of CRC and possibly polyps.

METHODS: We reviewed all colonoscopies performed at our institution from January to December 2007. Patient data were collected on age, sex, tobacco and alcohol history, and the presence of colon lesions.

RESULTS: Our data included 663 patients (643 men and 20 women) with a mean age of 60.7 years (range 23–89 years); 68.5% were current/former tobacco users, 53.7% were current/former alcohol users, 37.6% had used both, and 21.7% had used neither. Colonoscopy findings were as follows 64% of patients had no lesions, 30.6% had tubular polyps, 3.5% had villous polyps, and 2% had cancer. The current use of tobacco, alcohol, or both was associated with the early development of colon pathology (ie, 66.9 years, 61.1 years, and 59.2 years [P < .05], respectively). In nonusers, the mean age was 67.7 years.

CONCLUSIONS: Our work confirms that the use of alcohol and tobacco is associated with an earlier onset of colon pathology. Consideration should be given to modifying screening guidelines to include these habits as “high-risk” factors.

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Colorectal cancer (CRC) is the second leading cause of cancer deaths for men and women combined in the United States and the fourth worldwide.12 It is estimated that in the year 2012 9% of deaths from cancer will be attributed to CRC.1 The symptoms of CRC set in over the course of years. These changes often go unrecognized or are dismissed as nothing more than signs of normal aging.

The widespread adoption of screening guidelines allowing for the early detection and removal of precancerous polyps has led to a corresponding decline in the incidence of CRC.1-3 Since 1998, the incidence has decreased 3% per year in men and 2.3% per year in women.4 However, it is worth noting that the incidence of CRC has increased 1.7% per year since 1992 for adults younger than 50 years of age for whom screening is not indicated.1,5

The goal of CRC screening in asymptomatic individuals is to identify and remove certain types of polyps before they become malignant.6 Polyps may be classified as non-neoplastic and neoplastic. Non-neoplastic polyps include hamartomatous, juvenile, hyperplastic, and inflammatory polyps. All of these are considered to have no malignant potential. Neoplastic polyps are adenomas that may be divided into 3 histologic categories, the most common of which is the tubular adenoma.
Tubular adenomas account for roughly 75% of all neoplastic polyps. About 5% of these harbor malignant cells. Intermediate, or tubulovillous, adenomas account for 15% of neoplastic polyps and 22% contain malignant cells. Villous adenomas, although representing only 10% of neoplastic polyps, have the highest malignant potential with 40% harboring malignancy.

The size of the polyp is directly correlated with the presence of dysplasia or malignancy. Polyps greater than 10 mm have roughly a 3% chance of containing invasive carcinoma, whereas polyps smaller than 5 mm have a frequency of invasive carcinoma approaching 0% to .05%. It may take 5 to 10 years for normal mucosa to develop into a visible polyp, followed by another 2 years to 3 years during which time the polyp may become malignant.

Current American Cancer Society screening guidelines recommend initial CRC screening for average-risk individuals at age 50. The American Cancer Society further dictates that the age of the initial screening may be adjusted downward to age 40 if the patient has a first-degree relative with CRC or a polyp at age greater than or equal to 60 years or 2 or more second-degree relatives with CRC. If the patient has a first-degree relative with CRC or a polyp at an age less than 60 years or 2 or more first-degree relatives with CRC, screening is to begin at age 40 or at an age 10 years younger than that of the youngest family member at the time of diagnosis, whichever comes first.

Modifiable risk factors for CRC include diets low in fiber or high in red meat and fat, obesity, a sedentary lifestyle, alcohol consumption, and smoking. Tobacco use has been reported to have a strong, consistent relationship with colorectal adenomas and carcinomas.

A positive dose effect has also been shown between alcohol and CRC. The exact pathological mechanism is unknown, but it is suspected that the alcohol metabolite acetaldehyde may be a crucial player. It may contribute to the formation of free radicals and the proliferation of mucosal tissue.

The combination of current smoking, specifically long-term, with moderate to heavy alcohol use has been reported to have more significant effects. In 2 recently published database reviews, concomitant alcohol and tobacco use were associated with an earlier onset of CRC. We hypothesized that the use of alcohol and tobacco would also be associated with the earlier development of premalignant polyps. Therefore, we retrospectively evaluated a group of patients undergoing screening colonoscopy at our institution.

Results

A total of 670 patients underwent colonoscopies between January 1, 2007, and December 31, 2007, at the Central Arkansas Veterans Affairs Hospital. Twelve patients were excluded from the study because their colonoscopies were not completed (n = 4) or they had no social history available for review (n = 4). Six hundred sixty-three patient charts were reviewed.

The average age at the time of colonoscopy was 60.7 years, ranging from 23 to 89 years. Six hundred forty-one patients (96.7%) were male veterans; the other 22 patients (3.3%) were women. A total of 454 patients (68.5%) had used or were currently using alcohol. Only 144 patients (21.7%) had used tobacco only, alcohol only, both, and neither. Using Stata 11 (StataCorp LP, College Station, TX), we performed univariate analysis with the t test for age and univariate analysis with chi-square tests for tobacco use, alcohol use, and sex. We ran a linear regression to evaluate the relationship between the finding of colorectal pathology, the age at diagnosis, and the current and former use of alcohol and tobacco.

Methods

We obtained institutional review board approval to retrospectively review the records of 671 patients at the Central Arkansas Veterans Healthcare System, Little Rock, AR, who had a colonoscopy performed by a staff surgeon from January to December 2007. Exclusion criteria from the study were an incomplete colonoscopy or no documentation of social history. We collected data on age, sex, tobacco use, and alcohol use in addition to data on the pathology of specimens taken during the colonoscopy. Our age variable represented the age of the patient at the time of the colonoscopy. Our tobacco and alcohol variables were binary variables. The tobacco variable was positive if a patient had a prior or current history of smoking at least 1 pack per day. The alcohol variable was positive if the patient had a prior or current history of 3 or more alcoholic beverages per day.

Colonoscopy specimens were placed into 1 of 4 categories: no lesion or benign finding, tubular adenoma, tubulovillous adenoma, and invasive cancer. For each group with pathology, we calculated the average age at presentation for those who used tobacco only, alcohol only, both, and neither. Using Stata 11 (StatCorp LP, College Station, TX), we performed univariate analysis with the t test for age and univariate analysis with chi-square tests for tobacco use, alcohol use, and sex. We ran a linear regression to evaluate the relationship between the finding of colorectal pathology, the age at diagnosis, and the current and former use of alcohol and tobacco.
at an average age of 67.7 years. Most patients (48.1%) used both tobacco and alcohol at the time of presentation.

Univariate analysis using the t test and the chi-square test was performed comparing the mean age, sex, and tobacco and alcohol use of patients with and without dysplastic or cancerous lesions (Table 2). The mean age at presentation was statistically significantly greater for patients with premalignant lesions ($P < .05$). Tobacco use was statistically significantly elevated in patients with dysplastic or cancerous lesions ($P < .05$). Alcohol use and sex were not significantly different for both groups ($P > .05$).

Analyzing the subset of patients who had a premalignant or malignant lesion at the time of the colonoscopy with the univariate t test revealed that there is a statistically significant difference in the age at presentation with dysplasia or cancer if a patient has smoked, used alcohol, or both ($P < .05$) (Table 3). Finally, we performed multivariate analysis with linear regression using the presence or absence of dysplastic lesions and cancerous lesions as our dependent variables (Table 4). Patients with advanced age, current or prior tobacco use, and current or prior alcohol use all had a greater incidence of dysplasia or cancer on colonoscopy. Only age and tobacco had a statistically significant odds ratio ($P < .05$). Our tobacco-alcohol interaction variable was not significant ($P > .05$).

**Comments**

Alcohol and tobacco use are 2 of several epidemiologic factors shown to have concordance with increased formation of both colorectal carcinoma and adenomas, which are known precursors to cancer.\textsuperscript{24,30,32} Tobacco use has a strong, consistent relationship with colorectal adenomas,\textsuperscript{21,31,32} and the withdrawal of tobacco has been reported to significantly reduce the odds of the development of both hyperplastic polyps and adenomas.\textsuperscript{34} Smoking has also been shown to be an important risk factor in both the formation and increased size of adenomatous polyps.\textsuperscript{29} Pooled risk estimates for current, former, and ever smokers compared with never smokers showed a higher risk of adenomas in those with exposure to tobacco and a stronger association for high-risk adenomas than low risk.\textsuperscript{29,33} Ever smokers were 18% more likely to be diagnosed with CRC than never smokers. This was significant for those with a smoking history greater than 30 years and was dose dependent. Those who had ever smoked were 25% more likely to die from CRC than those who had never smoked.\textsuperscript{29}

Our data suggest that there is an association between increasing age, previous or current tobacco use, and the development of dysplasia or cancer evident on colonoscopy.
This was shown to be statistically significant, both with multivariate analysis (linear regression) and univariate analysis (the t test and the chi-square test). Both age and tobacco use are independent risk factors for the development of dysplasia.

It is important to mention that although the dose of tobacco was not quantified, it was still an independent and significant risk factor for premalignant or malignant lesions. Therefore, exposure to tobacco, independent of the dose, has a causal relationship with the development of dysplasia or cancer.

The role of alcohol in colorectal tumorigenesis has been debated. There are reports that low to moderate levels of alcohol may have a protective effect against the development of colorectal adenomas although with heavy intake this effect is lost. Moderate to heavy alcohol consumption has been shown to be an independent risk factor in men for the progression from adenomas to carcinomas.

Univariate analysis of the subset of patients who had a premalignant or malignant lesion suggested that patients who use or used alcohol, tobacco, or both are younger at presentation (P < .5). This was independent of the dose of alcohol and tobacco. Although univariate analysis revealed a correlation between positive alcohol history and dysplasia, this was not statistically significant when applying logistic regression. Tobacco and alcohol use may precipitate the development of dysplasia or cancer (Tables 1 and 3). When applying the interaction term to both variables, it seems that the effects of these 2 factors are simply additive.

Our data are limited in several respects. We recognize that our veteran population is unique and may not reflect true population based on a female-to-male ratio, smoker-to-non smoker ratio, or the combination of smoking and drinking. Also, our database includes all colonoscopies for a year and does not distinguish between screening and diagnostic procedures. In addition, we did not collect data on whether these patients previously had a colonoscopy and how recently. Patients with better health habits might be more likely to have participated in screenings and might have previously had polypectomy; these patients might have erroneously been placed into a no-lesion group.

Conclusions

Despite the limitations, our data do indicate that alcohol and cigarette use can lead to an earlier presentation of colorectal premalignant and malignant lesions. To confirm this, we would hope to study this further in a larger population across more than 1 institution. We would also better quantify the size of the lesions and the amount of exposure to alcohol and tobacco. Current colorectal cancer guidelines do not consider lifestyle risk factors when recommending early “high-risk” patient screening. We propose a trial of screening both male and female patients between 40 years and 50 years old who consume significant alcohol and/or tobacco to assess the incidence of colorectal polyps in this subset of patients. Based on these results, the screening guidelines could be modified to include patients with these lifestyle risk factors as being at a higher than average risk. The earlier screening of this new subset of “high-risk patients” may lead to an earlier detection of premalignant lesions and decrease subsequent morbidity and mortality from the development of colorectal cancer.

References

Discussion

Dr Eugene Foley (Madison, WI): Thank you Dr Rueda for your comments. To answer your first question, in our study we just included all colonoscopies. We did not actually divide it into screening or diagnostic colonoscopies. If that is true, do you think or are you concerned about the addition of these diagnostic colonoscopies into this if you are really asking questions about screening? The second question is did you collect any information about family history? Your study shows very nicely that there were clinically significant advanced polyps or cancer in that early (ie, around 50 years of age) group who might have had to undergo colonoscopies starting let's say at the age of 40, is really going to help, you would expect that there were clinically significant advanced polyps or cancers in the group of patients between 50 and 55 years of age. Could you expand a little bit? What was the number of patients in that early (ie, around 50 years of age) group who might have had polyps detected and removed with some improvement in clinical outcome if they had been screened as 40 year olds?

Dr Mario Rueda (Little Rock, AR): Thank you Dr Foley for your comments. To answer your first question, in our study we just included all colonoscopies. We did not actually divide it into screening or diagnostic colonoscopies. We are planning on performing further studies on this in which we actually divide these 2 groups of patients and examine those who had screening colonoscopies separately. We were interested in any pathology found in these different
groups of patients and that is why we decided to include all the colonoscopies that were performed during that year. In regards to your second question, we did not actually collect any data on family history because it was not available for all of our patients, but it is something we are planning to include in our data in the future. In regards to the pathology for the polyps, we actually labeled them only on their final pathology results as either adenomas or malignancy or benign polyps, but we did not actually assess their size, if it was a recurrent polyp, or any other clinical features that would suggest increased malignancy. That will be something I will be very interested in incorporating in future studies.