Consumption of Wine for Prevention of Colorectal Cancer

Sean Naylor

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Abstract
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Method: An exhaustive search was performed of available medical literature from 2000 to the present for studies that investigated wine consumption and diagnosis of colorectal cancer. The reviewed studies were examined for quantities of wine consumed and trends in colon cancer and rectal cancer incidence.

Results: The examination of the three studies in this review failed to find consensus in the relationship between wine consumption and colorectal cancer. Both protective and deleterious effects are suggested, though these relationships were most often not statistically significant.

Conclusion: Due to inconsistent relationships between studies, no confidence can be placed in a recommendation for or against drinking wine as a means of preventing CRC. Evaluation of the evidence reviewed here using the GRADE system indicates that future studies will likely improve knowledge about whatever relationships between wine consumption and CRC may exist.

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Torry Cobb

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Consumption of Wine for Prevention of Colorectal Cancer

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Annjanette Sommers MS, PAC
Biography

Writing anything of meaning here feels less biographical and more like an obituary. And I truly hope it is not time for that just yet.

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[Redacted for privacy]
ABSTRACT

Background: Development of colorectal cancer (CRC) has been linked to several lifestyle factors including alcohol consumption. Less well understood is the relationship of wine consumption to the development of CRC. Among the purported health benefits of wine consumption there is evidence of in vitro suppression of colon cancer cells, but these studies lack clinical validation. This systematic review aims to determine the clinical outcomes of wine consumption on the development of CRC and use the GRADE system to evaluate the available evidence regarding this outcome.

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Results: The examination of the three studies in this review failed to find consensus in the relationship between wine consumption and colorectal cancer. Both protective and deleterious effects are suggested, though these relationships were most often not statistically significant.

Conclusion: Due to inconsistent relationships between studies, no confidence can be placed in a recommendation for or against drinking wine as a means of preventing CRC. Evaluation of the evidence reviewed here using the GRADE system indicates that future studies will likely improve knowledge about whatever relationships between wine consumption and CRC may exist.

Keywords: Colorectal cancer, alcohol consumption, wine consumption
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INTRODUCTION

Background

Though declining over the past 20 years the death rate from colorectal cancer (CRC) ranks second among all cancers in adults excluding skin cancers when counted together (American Cancer Society [ACA], 2010). This decline is largely attributed to more advanced screening techniques that allow for the detection and removal of polyps in addition to public health initiatives aimed at encouraging early screening. Advances in research have shown that both genetic factors as well as environmental exposures play a role in the development of CRC. This research has, in turn, increased public awareness and helped mitigate some of these factors (Chan & Giovannucci, 2010). Despite these efforts, the lifetime risk of developing CRC for both men and women remains near 5% (ACA, 2010).

The results of several population-based studies have suggested that factors such as diets low in fiber and high in saturated fats, a sedentary lifestyle, and cigarette smoking have a strong association with colorectal cancer (Chan & Giovannucci, 2010; Hermann, Rohrmann & Linseisen, 2009; Kirkegaard et al., 2010). The role of alcohol consumption in the development of CRC has been examined also (Hermann et al., 2009; Pöschl & Seitz, 2004). While it appears certain that, at high levels of consumption, the consumption of alcoholic beverages is associated with the development of CRC, the relationship is less well known when alcohol is consumed infrequently or in moderate amounts (Park et al., 2010). Studies that examine the relationship between alcohol use and
CRC often do not delineate whether or not study participants consumed wine, beer, or spirits and in what relative amounts each are consumed, thereby making it difficult to determine if there is a differential causal relationship between types of alcoholic beverage consumed and the development of CRC.

The role that wine consumption plays in the development of CRC has been questioned in recent years. While the consumption of wine has been shown to have some positive health effects, its role in the prevention of cancer remains less clear (Visioli, Grande, Bogani, & Galli, 2004; Vislocky & Fernandez, 2010). Several theoretical models propose that constituents of wine reduce colorectal neoplasia and cancer. Polyphenols, a natural component of grapes and consequently wine that have been shown to have an anti-proliferative effect on colon cancer cells in vitro (Kim et al., 2006; Scheider et al., 2000). Because these studies lack clinical evaluation, it is difficult to determine to what extent wine consumption may affect the incidence of CRC in the general population.

Purpose of the Study

This review aims to determine if wine consumption has a preventative effect against the development of CRC through an examination of the available evidence in the literature and determining what the quality of evidence for that outcome is by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool developed by the GRADE Working Group.

METHODS
An extensive literature search was performed using PubMed, Medline, Cochrane Systematic Reviews and CINHAL. These databases were accessed through the Pacific University Library system. The keywords searched included “colorectal neoplasms,” “colorectal cancer” and “wine” individually and in combination. The search was limited to human subjects, the English language and articles published since the year 2000. The initial results included 87 articles. Reviews, narrative articles, case studies, duplicate articles and those articles not pertaining to relevant clinical outcomes were excluded. This process yielded 4 articles to review of which 3 could be recovered in full text form.

RESULTS

Chao et al. (2010)

This prospective, multiethnic, observational cohort study of men in the California Men’s Health Study sought to establish relationships between alcohol intake, particularly red wine intake, and colorectal cancer occurrence. Eligible study participants included men aged 45-69 years enrolled in the Kaiser Permanente (KP) California health plans in January, 2000. Information about several aspects of health including diet patterns, activity level and socio-economic status was gathered from 84,170 men who completed mailed questionnaires. Men who reported any previous cancer history and those diagnosed as having CRC within 6 months after beginning surveillance were excluded, leaving 77,371 respondents. The primary analytical sample was restricted to the 43,483 men who had been continuously enrolled in KP during the years 1998-2002 to account for their endoscopy utilization during the time
period leading up to the study. Those who had previous endoscopic exams were further subdivided into groups of those who had received the exam for screening or those who had been evaluated for specific symptoms. Alcohol consumption was gauged by asking the participants to categorize their drinking pattern of beer, red wine, white wine or spirits into the following categories: never or less than once per month, 1-3 drinks per month, 1 drink per week, 2-4 drinks per week, 5-6 drinks per week, 1 drink per day, 2-3 drinks per day, 4-5 drinks per day, or 6+ drinks per day. For red wine drinkers these categories were then grouped as follows: non-drinker, <1 drink per week, ≥1 drink per week, <1 drink per day, and ≥1 drink per day. From these results each study participant’s total daily alcohol intake across types was also calculated. Follow-up began at the time of survey submission and ended at the time of CRC diagnosis, diagnosis of other cancers, termination of health plan membership, death or the end of the year 2007, whichever came first. The median follow-up time was 5.3 years.

In the crude analysis of all 73,371 men in the study which included 287 cases of CRC, the hazard ratio when compared to non-drinkers was identical for each type of alcoholic beverage consumed, including 1.00 (1.00-1.01) for beer, 1.00 (0.99-1.01) for red wine, 1.00 (0.99-1.01) for white wine, 1.00 (1.00-1.01) for liquor and 1.00 (1.00-1.01) for all types of alcohol combined. For all colorectal cancer cases in people drinking greater than one glass of red wine per day the hazard ratio was 1.16 (0.56-2.40). For those cases presenting as Stage I or II cancer, the hazard ratio for drinking at least one glass of red wine per day was 1.70 (0.68-4.29) and 0.81 (0.19-3.55) for those with Stage III or IV cancer.
hazard ratio for having at least one glass of red wine per day and the development of colon cancer was 1.02 (0.40-2.65) and 1.40 (0.43-4.54) for rectal cancer. The authors concluded that there was no clear relationship between the consumption of red wine and colorectal cancer at any intake level. They also point out that their findings did not show a dose-response relationship between total alcohol consumption and CRC.

Pedersen, Johansen and Grøbæk (2003)

This population-based, observational cohort study was performed with members of the Copenhagen Centre for Prospective Population Studies to determine the effects of different types of alcohol consumption on the development of colorectal cancer. The cohort was recruited from the years 1964 to 1976 and included 14,662 women and 18,602 men. Participants completed a health questionnaire including information about alcohol consumption, smoking history, education, diet and leisure activity. Alcohol consumption was divided into categories by types of alcohol consumed (beer, wine, spirits) and number of drinks per week (<1, 1-6, 7-13, 14-27, 28-40, and >41). Using data from the Cancer Register and the National Patient Register in Denmark those subjects with prior history of CRC, Crohn’s Disease or Ulcerative Colitis, or those without complete information regarding alcohol intake were excluded leaving the total number of people included in the analysis to 15,491 men and 13,641 women. Subjects were followed from time of survey submission to death, emigration, disappearance, time of diagnosis of colon or rectal cancer, or January 1999, whichever came first. Mean follow-up time for study participants was 14.7 years,
during which time 411 cases of colon cancer and 202 cases of rectal cancers occurred in the study population.

No association was found between total alcohol intake and colon cancer even when more than 41 drinks per week were consumed (ARR 0.8, 95% confidence interval 0.5-1.5). There was, however, an association between those who consumed more than 41 drinks per week and rectal cancer (RR 2.2, 95% confidence interval 1.0-4.6). In people who consumed >1 drink of wine per week, a borderline statistically significant decrease in colon cancer was noted (RR 0.9, 0.7-1.1), while no difference was noted in those drinking beer and spirits. For those who drank >14 glasses of wine per week, the relative risk was also decreased (0.5, 0.2-1.0), but the relationship remained insignificant. There was a slight statistical association in rectal cancer for those drinking more than 14 drinks per week of beer (RR 1.4, 0.8-2.4) or spirits (RR 1.3, 0.6-3.0), as well as a non-significant association in rectal cancer with more than 14 drinks per week of wine (RR 0.9, 0.4-2.1). Among those who drank different types of alcohol, those who drank more than 14 drinks per week of beer and spirits but no wine had a relative risk of 3.5 (1.8-6.9) for developing rectal cancer while those who had more than 14 total drinks per week with at least 30% of their alcohol intake being wine had a relative risk of 1.8 (1.0-3.2). The authors concluded that a dose-response relationship between the consumption of alcohol and an increased incidence of rectal cancer does exist, but found no association between colon cancer and alcohol consumption. Additionally, as the risk of rectal cancer was
limited to drinkers of spirits and beer, they also concluded that wine may have an anticarcinogenic effect.

Sharpe, Siemiatycki, and Rachet (2002)

This population based case-control study was performed between 1979 and 1985 at multiple hospitals in Montréal, Canada and involved only men 35-70 years of age. During this time 911 cases of CRC were discovered, of which 754 responded to a request for information about prior health history and, specifically, alcohol consumption. Face-to-face interviews were completed whenever possible, but authors also gathered information from spouses when the subject was too ill or recently deceased. Questions asked included those regarding the frequency and type of alcohol consumption along with other health and socio-economic questions such as smoking history, education level, and yearly income. Of the group that responded to the request for information, 160 cases were excluded either because they refused the interview or because the authors felt that adequate information had not been gathered. Nine other cases were excluded because cancer had been identified in multiple bowel locations, leaving 585 total cases for further evaluation. These cases were then categorized according to whether the cancer site was in the proximal colon, the distal colon, or the rectum. The authors selected 500 population controls by using an electoral database and random number dialing from which data regarding alcohol and health status was gathered in a similar fashion as was done for the cases. These controls were then matched to cases by age and area of residence,
Among those study participants who drank more than 5 drinks per day the odds ratio of developing distal colon cancer was 3.0 (1.6-5.6) and 2.0 (1.1-3.6) for rectal cancer, which is in contrast with the findings for the proximal colon (OR 1.6, 0.9-2.9). Analysis of the consumption of each type of alcohol individually revealed that drinking more than 5 beers per day was found to have an association with the occurrence of proximal colon cancer (OR 2.4, 1.2-4.6), distal colon cancer (OR 2.4, 1.3-4.6) and rectal cancer (OR 1.8, 1.0-3.1). No association was found for consumption of more five drinks of spirits per day in the proximal colon (OR 2.0, 0.9-4.7), distal colon (OR 1.3, 0.5-3.3), or rectum (OR 1.9, 0.9-3.9). The authors note a statistically insignificant association in rectal cancer (OR 0.2, 0.0-1.1) and proximal colon cancer (OR 0.7, 0.2-1.4) for those who drank more than 5 glasses of wine per day, but no association in the rate of distal colon cancer (OR 1.1, 0.4-3.6) was found. The authors concluded that daily consumption of alcohol caused an increase in occurrence of rectal and distal colon cancer, but not proximal colon cancer, especially with heavy beer drinking. Despite the absence of a significant association the authors note a possible protective effect of drinking wine on both colon and rectal cancer.

DISCUSSION

The findings of the studies included in this review seem to add credence to previous conclusions about the positive association between alcohol consumption and the development of CRC, especially in the incidence of rectal cancer. They also show that while there may be some relationship between wine...
consumption and CRC, the nature of this relationship is less than clear. Sharpe et al. (2002) found an insignificant trend towards a protective function of wine in the colon and rectum. Pedersen et al. (2003) found a similar trend along with the lone significant value found in this review regarding wine’s possible protective effect against rectal cancer when wine was consumed as a significant portion of a given person’s overall alcohol intake. In contrast to these two studies, Chao et al. (2010) found no significant trends in incidence of CRC irrespective of frequency or quantity of red wine consumption, and highlight a possible trend towards increased incidence of colon and rectal cancer with frequent red wine consumption. In light of the relative dearth of consistent relationships between wine consumption and CRC incidence in the studies reviewed, and because of disagreement between the studies about what conclusions can be drawn about the role of wine consumption in CRC, it is difficult to make any firm judgments about what the totality of the available data could signify.

Study Limitations

Identifying the limitations of these studies helps elucidate some of the potential reasons why there is difficulty associated with making conclusions based on the data presented. One factor the authors of each study point to as a reason why statistical power was limited for making conclusions is the relatively small numbers of CRC cases encountered in these studies. The confidence
intervals are wider than would otherwise be expected from studies with so many participants, but this is suggested to be a direct reflection of the limited number of cases of CRC that were discovered. However, a large sample size does indicate that a statistical relationship would be more likely to be apparent if in fact there is a true relationship should the outcome detected actually be caused by the intervention being examined. In this review the lack of statistical relationships between colorectal cancer and wine consumption most likely has less to do with the few number of cases observed and more to do with the possibility that there does not exist a relationship between CRC and wine consumption given the fact that the sample sizes were so large.

Another limitation that each study reports is the potential for bias in the self-reporting of one’s own alcohol consumption. The authors point at the inherent difficulty of gathering information about a person’s health status and especially alcohol consumption from self-reporting, whether or not the information was gathered by personal interview or questionnaire. Though the authors of these studies believe the potential for this type of error to be relatively small they do identify the potential for underreporting of alcohol consumption as a means of obfuscating what relationship may actually exist between wine consumption and CRC. Further confusing the issue is that all three studies point out the difficulty of not only assessing a person’s current alcohol intake but also past and future alcohol intake. Sharpe, Siemiatycki, & Rachet (2002) did obtain an estimate of lifetime alcohol consumption for each subject, but caution that this data may be unreliable due to poor patient recollection. The other two studies
simply caution about inferring a person’s past alcohol status if they self report as being non-consumers presently, and that the subject may have an extensive alcohol consumption history but is currently a non-consumers and are thus analyzed as non-consumers (Chao et al., 2010; Pedersen, Johansen, & Grøbæk, 2003).

Examination of the subject characteristics in these populations also reveals potential limitations of the studies. First, in this review only Pedersen, Johansen and Grøbæk (2003) examined female subjects, and as such what little can be said about the outcome being evaluated is likely less applicable to women than men. Second, none of these studies account for the presence or absence of family history of CRC. While they do exclude patients with ulcerative colitis or Crohn’s Disease, both of which are risk factors for CRC, no study in this review attempts to account for family history of CRC in their analysis. Both of these limitations further limit what can be inferred about the data presented.

Evaluation of Evidence Using GRADE

In this review the GRADE system was used to evaluate the outcomes of both colon cancer and rectal cancer based on wine consumption. GRADE initially places evidence into categories based on whether or not the study was an observational study or a randomized controlled trial. If the outcome in question is based on observational studies such as those in this review, then the initial grade of evidence for that outcome is “low,” whereas for randomized
controlled trials the initial grade is “high” (Guyatt et al., 2008). A “low” grade implies that although the effect of an outcome may be shown to be significant, “future studies about that outcome are likely to lead to a change in the estimate of that effect” (Guyatt et al., 2008, p. 926). After being assigned an initial grade, each outcome is then evaluated by what degree the evidence used to generate the outcome meets certain criteria viewed as instrumental to the validity of the study. The criteria are overall study quality, consistency of outcome, directness of comparisons, precision of data and presumed publication bias. If any of the studies used are found to be significantly lacking in these areas, the overall grade of the outcome can be decreased (Guyatt et al., 2008). Because downgrading does not apply to observational studies both outcomes were given an initial grade of “low” because they were based completely on three observational studies.

The GRADE system also evaluates an outcome based on other criteria that can possibly increase the grade of the effect of an outcome in observational studies. The criteria include whether or not there was a large magnitude of effect observed, if there was a dose-response relationship in the outcome, and whether or not potential confounders were accounted for in the analysis. If any of the studies evaluated meet one or all of these criteria, the grade of the outcome may be increased to “moderate” or “high.” A “moderate” grade implies that future research may change confidence in the effect of an outcome, while a “high” grade implies that future research is unlikely to change confidence in the effect of an outcome (Guyatt et al., 2008). When each outcome in this review was
analyzed neither was eligible for elevation to a higher grade based on the above criteria.

Conclusions

Because evaluation of each outcome failed to necessitate an elevated grade, both received a final grade of “low.” The GRADE system was then used to grade the overall base of evidence, and because both outcomes individually received “low” grades, the over all grade was, in turn, “low.” As such, it is likely that future study of the relationship between CRC and wine consumption will lead to a better understanding of whether or not wine has either protective or provocative effects on CRC. Though at present the relationship of alcohol in general, especially beer and spirits, to CRC may be clearer, the effects of wine consumption specifically on CRC is not fully known, and caution should be exercised when advising patients on what health benefits actually exist from drinking wine.

REFERENCES


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<td>development of colon cancer 2 cohort studies, 1 case-control study</td>
<td>no statistical association</td>
<td>Low 0 0 0 0 0 0 0 Low</td>
<td>Low</td>
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