Reduced Coffee Consumption Among Individuals With Primary Sclerosing Cholangitis but Not Primary Biliary Cirrhosis

Craig Lammert,* Brian D. Juran,* Erik Schlicht,* Xiao Xie,‡ Elizabeth J. Atkinson,‡ Mariza de Andrade,‡ and Konstantinos N. Lazaridis*

*Division of Gastroenterology and Hepatology and ‡Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, Minnesota

BACKGROUND & AIMS: **Coffee consumption has been associated with decreased risk of liver disease and related outcomes. However, coffee drinking has not been investigated among patients with cholestatic autoimmune liver diseases, primary biliary cirrhosis (PBC), or primary sclerosing cholangitis (PSC). We investigated the relationship between coffee consumption and risk of PBC and PSC in a large North American cohort.**

METHODS: **Lifetime coffee drinking habits were determined from responses to questionnaires from 606 patients with PBC, 480 with PSC, and 564 healthy volunteers (controls). Patients (those with PBC or PSC) were compared with controls by using the Wilcoxon rank sum test for continuous variables and c^2 method for discrete variables. Logistic regression was used to analyze the estimate of the effects of different coffee parameters (time, frequency, and type of coffee consumption) after adjusting for age, sex, smoking status, and education level.**

RESULTS: **Patients with PBC and controls did not differ in coffee parameters. However, 24% of patients with PSC had never drunk coffee compared with 16% of controls ($P < .05$), and only 67% were current drinkers compared with 77% of controls ($P < .05$). Patients with PSC also consumed fewer lifetime cups per month (45 vs 47 for controls, $P < .05$) and spent a smaller percentage of their lifetime drinking coffee (46.6% vs 66.7% for controls, $P < .05$). These differences remained significant in a multivariate model. Among PSC patients with concurrent ulcerative colitis, coffee protected against proctocolectomy (hazard ratio, 0.34; $P < .001$).**

CONCLUSIONS: **Coffee consumption is lower among patients with PSC, but not PBC, compared with controls.**

Keywords: Caffeine; UC; Risk Factor; Cholestasis; Biliary Inflammation.

The robust stimulant qualities of coffee have been enriching human vitality since its incarnation; however, only recently have specific health benefits of this brew been reported in the scientific literature. Coffee is now considered as a medically beneficial beverage because of inverse associations with metabolic syndrome,[1] cardiovascular disease,[2] and weight gain,[3] despite previous reports.[4] A recent study by Freedman et al[5] revealed a strong inverse dose-dependent relationship between coffee consumption and total and cause-specific mortality.

Coffee attributes extrapolate to chronic liver disease as well; multiple studies during the last 20 years support an association between coffee consumption and decreased risk of liver disease. A sentinel study specific to alcoholic liver disease revealed an inverse relationship between coffee and risk of liver cirrhosis.[6] Subsequently, coffee was linked to more favorable liver tests in high-risk patients,[7] as well as decreased mortality in patients with cirrhosis.[8] Recently, improved liver-related outcomes and reduced hepatic fibrosis were seen in viral hepatitis C patients who consumed 2 coffee-cup equivalents per day.[9] Last, a recent meta-analysis revealed approximately 40% risk reduction for hepatocellular carcinoma among individuals who drink coffee and 50% risk reduction for those who drink coffee heavily compared with nondrinkers.[10]

Despite population-based associations between coffee and liver disease risk and outcomes, an examination between coffee consumption and cholestatic liver disorders

Abbreviations used in this paper: CCA, cholangiocarcinoma; CD, Crohn's disease; HR, hazard ratio; IBD, inflammatory bowel disease; MCLD, Mayo Cholestatic Liver Disease; MCPGE Registry, Mayo Clinic PBC Genetic Epidemiology Registry; MCSC, Mayo Clinic Survey Center; PBC, primary biliary cirrhosis; PROGRESS, PSC Resource Of Genetic Risk, Environment and Synergy Studies; PSC, primary sclerosing cholangitis; PSC-CD, concurrent PSC and CD; PSC-UC, concurrent PSC and UC; UC, ulcerative colitis.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2013.12.036

is currently lacking. Primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) are both chronic autoimmune liver diseases characterized by biliary inflammation leading to biliary fibrosis and subsequent cirrhosis, liver transplant, or death.[11–13] To date, the pathogenesis of PBC and PSC remains unclear, although both likely involve numerous complex interactions between predisposing genetic alleles and environmental exposures. Prior reports of fibrosis mitigation in other chronic liver disorders led us to hypothesize that coffee consumption exerts a protective role in the development of PBC and PSC. In the current study we aimed to assess patterns of coffee consumption among a cohort of PBC and PSC patients and controls drawn from our own medical center.

Methods

Study Populations

The Mayo Cholestatic Liver Disease (MCLD) resource (Figure 1) includes PBC and PSC patients obtained from 2 cohorts recruited at our medical center as a part of the (1) Mayo Clinic PBC Genetic Epidemiology (MCPGE) Registry[14,15] and (2) PSC Resource Of Genetic Risk, Environment and Synergy Studies (PROGRESS).[16] These resources were established with the aim of elucidating the genetic and environmental contributors to PBC and PSC pathogenesis. PBC and PSC patients met clinically accepted standards of each diagnosis.[17] Controls were serially recruited from the Mayo Clinic Division of General Internal Medicine during annual visits for preventive medical examination. Moreover, all controls and cases were tested for anti-mitochondrial antibodies and alkaline phosphatase in serum at the time of enrollment. Control exclusion criteria included evidence of prior or current liver disease. Informed consent was obtained from all the study participants. The present study and included cohorts conform to the ethical guidelines of the 1975 Declaration of Helsinki and have been approved by the Institutional Review Board of Mayo Clinic.

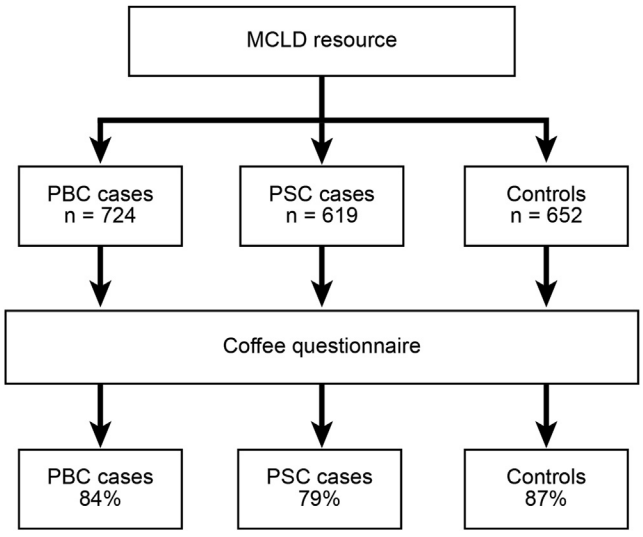

Figure 1. Participants and coffee questionnaire response rate within the MCLD resource.

Demographics, Medical History, and Lifestyle Assessment

At time of enrollment, cases and controls within the MCLD resource were supplied a study questionnaire directly or through the mail. This study instrument was developed by the Mayo Clinic Survey Center (MCSC) and collected information regarding demographics, medical history, and lifestyle exposures.[15] For instance, smoking was assessed, and a positive smoking history was defined as current or past smoking of $\geq$100 cigarettes during the patient's lifetime up until diagnosis of PBC or PSC,[18,19] or in the case of controls, up until completion of the questionnaire. A second questionnaire was mailed within 2 months of the initial contact in nonrespondents.

Coffee Assessment

To assess coffee consumption, patients within the MCLD resource were mailed a 2-page, scannable questionnaire that included a prepaid return envelope. This study tool, developed with the assistance of the MCSC, was composed of 10 questions highlighting current (ie, within the past 1 year) and past (ie, lifetime) coffee drinking habits. Coffee consumption was assessed by using 11 frequency categories, ranging from less than 1 cup per month to more than 9 cups per day. The questionnaire also obtained detailed information regarding coffee start and quit ages, if available, allowing assessment of average lifetime cups of coffee per month and percentage of lifetime consuming at least 1 cup of coffee per month. The total reported years consuming coffee and reported cup frequencies were used to calculate average lifetime cups of coffee. Percentage of lifetime consuming coffee was calculated by using age and reported duration of drinking at least 1 cup of coffee per month. Lifetime coffee status was classified by 3 separate categories: current, past, and never a coffee drinker. Parameters of coffee consumption were completed by totaling caffeinated and decaffeinated data. Participants who did not respond to the first mailing within 6 weeks were sent another coffee questionnaire.

Statistical Analysis

PBC or PSC patients were compared individually with a group of subjects (ie, controls) without evidence of PBC or PSC. Continuous variables were summarized by using medians and the 25th and 75th percentiles, and P values were obtained by using the Wilcoxon rank sum test. P values for discrete variables were obtained from the χ^2 test. Logistic regression was used to estimate the