Published in final edited form as:

J Rheumatol. 2013 September ; 40(9): 1498–1504. doi:10.3899/jrheum.121325.

ASSOCIATIONS OF ALCOHOL USE WITH RADIOGRAPHIC DISEASE PROGRESSION IN AFRICAN AMERICANS WITH RECENT ONSET RHEUMATOID ARTHRITIS

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Abstract

Objective—To investigate the associations of alcohol consumption and radiographic disease progression in African Americans with recently diagnosed rheumatoid arthritis (RA).

Methods—RA patients included in the study were participants in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis (CLEAR) registry. Patients were categorized based on self-reported alcohol consumption; those consuming < 15 beverages per month versus those with ≥ 15 per month. Association of radiographic disease progression over a one to three year period of observation with alcohol consumption was evaluated using multivariate generalized estimating equations.

Results—There were 166 patients included in the study, 39% reported that they had never consumed alcohol. Of the 61% who had consumed alcohol, 73% reported that they on average consumed less than 15 alcoholic beverages per month and 27% reported consuming ≥ 15 per month. In multivariate analysis, consumption of ≥ 15 alcoholic beverages per month was associated with an increased risk of radiographic disease progression ($p = 0.017$). There was no evidence of a relationship in those consuming < 15 beverages per month ($p = 0.802$).

Conclusion—There appears to be a dose-dependent relationship between alcohol use and radiographic disease progression in RA. Individuals who consume 15 or more alcoholic beverages per month may have accelerated rates of radiographic joint damage than with lower levels of consumption.

Keywords

Rheumatoid Arthritis; alcohol consumption; disease severity; disease activity

Introduction

African Americans with rheumatoid arthritis (RA) are a historically understudied population. However, recent efforts have begun to closely examine disease characteristics and risk factors within this group. An example is the study of tobacco use in African Americans with RA. Investigators have identified an increased risk of both autoantibody positive and autoantibody negative RA in African Americans who smoke tobacco. Furthermore, certain genetic variations including HLA-DRB1 shared epitope and N-acetyltransferase polymorphisms have been shown to potentiate smoking risk within this group of patients.(1,2) The complexity of RA, however, warrants investigation into other risk factors that may also be involved in the disease process. Alcohol consumption, for example, is a modifiable exposure that to our knowledge has not yet been studied in African Americans with RA.

To date, observational studies investigating the risk of RA associated with alcohol consumption have come predominantly from cohorts of European ancestry. Results from these studies suggest that low-to-moderate alcohol consumption is associated with a lower risk of developing RA.(3-5) However, a large prospective cohort evaluating 31,336 older women from Iowa found no such association between alcohol use and the risk of developing later-onset RA.(6) Differences in findings from these studies may reflect varying levels of alcohol consumption between European and American cohorts.

Indeed studies employing animal models of RA have shown that alcohol may exert paradoxical dose-dependent effects on disease pathogenesis. In select animal studies, investigators observed anti-inflammatory effects associated with alcohol intake characterized by lower levels of circulating pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor α (TNF- α). (7,8) Other studies, however, have shown that these anti-inflammatory effects may not be sustained with larger quantities of alcohol consumption.(9,10) A study comparing heavy drinkers with alcoholic liver disease to healthy controls with low/moderate levels of consumption found that pro-inflammatory circulating TNF- α levels were higher in the heavy alcohol consumption group.(10) Body mass index (BMI), however, was not controlled for in the analysis which may also influence TNF- α levels.(11) Based on these studies it is reasonable to infer that inflammatory cytokine levels may differ in patients with RA based on variability in alcohol intake and that this could potentially be reflected in disease activity.

A limited number of studies have examined disease progression in relation to alcohol consumption in patients with RA. A recent study investigated alcohol use and associations with radiographic progression in a European cohort with RA. This study demonstrated that low-to-moderate alcohol consumption was 'protective' against radiographic erosions, but heavy consumption was paradoxically associated with worse radiographic outcomes (12), consistent with the aforementioned biologic studies. It is difficult to conclude whether these results are generalizable to other cohorts. To date, there have been no studies investigating radiographic disease progression associated with alcohol consumption in African Americans with RA.

Although studies in African American cohorts have been limited, the potential effects may be particularly relevant because alcohol consumption appears to yield differing health effects in African Americans compared to Caucasians in the context of other inflammatory diseases.(13-17) Because of this, we sought to investigate whether similar effects of alcohol consumption are applicable in African Americans with RA. Specifically, our aim was to determine if alcohol consumption in African Americans is associated with radiographic disease progression during the early stages of RA.

Materials and Methods

Patient Population

Study participants were part of the Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis (CLEAR) registry.(18) All subjects self-reported African American race and satisfied the American College of Rheumatology (formerly, the American Rheumatism Association) 1987 classification criteria for RA (19), and had two years or less of disease duration from the initial onset of symptoms. Patients were enrolled from five participating academic medical centers in the southeast U.S. (University of Alabama at Birmingham, Emory University, University of North Carolina, Washington University, and the Medical University of South Carolina).

RA patients were enrolled between 2002 through 2005. At baseline, subjects received a complete history and physical examination and were asked to complete a participant questionnaire to gather demographic, diet, and general health information. Patients were then re-evaluated at a second time point three years (one to three years after enrollment) after disease onset using evaluations similar to those at enrollment. Since duration of follow-up varied among participants, follow-up time was controlled for in all analyses to limit potential confounding.

The study was approved by the Institutional Review Boards at each of the participating centers. All participants involved in the study provided informed written consent to participate.

Outcome and exposure measures

Radiographic disease progression was the primary outcome measure for this study. Radiographs of the hands, wrists, and feet were collected at baseline and at a second time point 3 years from disease onset. Radiographs were read with a known order of time. A modified Sharp/van der Heijde score (SHS) (20), was then computed by a single blinded observer using joint space narrowing and erosions totals as previously described.(21) SHS progression was then calculated by subtracting the baseline SHS from the follow-up SHS.

A detailed history of alcohol and tobacco use was collected at enrollment. Subjects were categorized into two groups: 1) subjects who reported either current or past use of alcohol, and 2) those that reported no prior history of alcohol use. Patients with a history of alcohol use provided the number of alcoholic beverages they consumed, on average, within a one-month time frame. The questionnaire did not define specific alcohol quantities or volumes that constituted a given alcoholic beverage. Smoking status was defined as never, former,

and current. Never smokers were those who reported < 100 cigarettes in their lifetime. Former smokers were those who smoked > 100 cigarettes in their lifetime but quit smoking prior to enrollment. Current smokers were those who reported smoking > 100 cigarettes and continued to smoke at the time of enrollment.

Demographic information including age, sex, and disease duration were collected at enrollment. Height and weight were also included to calculate body mass index (BMI, kg/m²) and patients were asked to report their annual income range and level of completed education. We categorized self-reported disease-modifying antirheumatic drug (DMARD) therapy at enrollment into six groups: 1) biologic agents (anakinra, etanercept, and infliximab), 2) hydroxychloroquine, 3) methotrexate, 4) other DMARDs (gold, penicillamine, sulfasalazine, leflunomide, azathioprine, cyclosporine, and cyclophosphamide), 5) combination therapy (patients concurrently receiving two non-biologic DMARDs), and 6) those not on any of these therapies. Groups were not mutually exclusive. Adherence and medication dispensing data were not collected but surveys were completed by trained study personnel with knowledge in DMARDs. Other biologics including adalimumab were not routinely available when the data was collected and therefore not included in the analysis. Since DMARD therapy was similar in the exposed and unexposed groups (Table 1) and because the number of patients on biologics was very small (7 patients), we subsequently classified DMARD use as a dichotomous variable comparing those receiving DMARD therapy versus those not receiving DMARD therapy for all subsequent analyses. Because of the potential risk channelling bias, methotrexate and methotrexate combination therapy were also analysed independently. Pain intensity was assessed by asking patients to rate their current level of pain (0 being no pain and 10 being the worst pain possible). Anti-CCP antibody positivity, rheumatoid factor (RF)-IgM positivity, HLA-DRB1 shared epitope (SE) positivity, and C-reactive protein were also collected as previously described.(22-24)

Statistical Analysis

Variations in patient characteristics at enrollment (age, disease duration, sex, education, income, DMARD use, methotrexate use, combination methotrexate use, HLA-DRB1 SE, anti-CCP antibody, and RF status) were compared for those with no history of alcohol and those who reported alcohol use using chi-square test for dichotomous variables and analysis of variance (ANOVA) for continuous variables.

The relationship of SHS and alcoholic beverages per month was initially examined using a running-line least-squares smoothing function as depicted in Figure 1. Upon visualization, it was clear that a natural break with an inflection in slope (checkmark shaped curve) was observed at ~15 alcoholic beverages per month. Patients were subsequently subcategorized into two groups based on consumption using a linear spline function with a knot at this break point. The low alcoholic beverage consumption group was defined as those consuming < 15 drinks per month including the non-drinker group and the heavier alcohol consumption group was defined as those who consumed ≥ 15 drinks per month. Radiographic disease progression (SHS scores) from baseline to year 3 from disease onset were then compared between the two groups using generalized estimating equation (GEE)

methods. A cut-off of two standard deviations from the mean was used to identify outliers and all subsequent analyses were repeated with the outliers excluded.

GEE models were structured using a first-order autoregressive correlation matrix to account for repeated measurements over time within the same individual. A quasilielihood under the independence model information criterion (QIC) measure was calculated for competing correlation matrices to confirm the structure.⁽²⁵⁾ As described in a previous study using data from CLEAR, our dependent variable (SHS) contained nonnegative integers with an over-dispersed Poisson-like distribution thus all GEE methods were fit with a negative binomial distribution.⁽²⁶⁾ Potential confounders were evaluated for an association with SHS using a univariate GEE model. Age, sex, disease duration and covariates with a *P* value less than 0.10 in the univariate analyses were included in the multivariate model. Time from baseline (< 2 years disease duration) to second visit (3 years from disease onset) was also included in the final analyses (time lapse between visits) to control for varied follow-up time between patients. Collinearity was tested using condition indices. All covariates had condition indices less < 30 and were therefore removed from the analysis. Lastly, because pain may be involved in the causal pathway and the present study was not powered to assess for an interaction, two models were generated, one with and one without pain as a covariate. No differences were observed and so pain was excluded from the final analysis. Statistical significance was set at $\alpha = 0.05$.

To determine if high alcohol intake precluded being on methotrexate and to investigate potential channelling as a source of bias we used a chi-square test to compare methotrexate use in the high alcohol group (≥ 15 beverages per month) versus the low alcohol group (<15 beverages per month).

Missing data may have occurred if patients did not report an answer on the patient questionnaire or if there was an error when analyzing a blood sample. There were 4 (2.4%) patients who reported alcohol use but did not provide an average number of alcoholic beverages per month. Additionally there were 2 (1.2%) patients without C-reactive protein information, 2 (1.2%) patients with missing data precluding BMI calculation, 2 (1.2%) without IgM-RF results, and 1 (0.6%) patient missing anti-CCP antibody status. To mitigate bias arising from stepwise deletion and to accommodate for missing values we imputed these data using multiple imputation by chained equations (ICE).

All statistical analyses were performed using Stata, version 10.1 (StataCorp. 2007. *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP).

Results

There were 166 patients included in the analyses with a mean ($\pm$ SD) age of 51 ($\pm$ 13) years. Of these, 86% were women, 68% were anti-CCP antibody positive, and 77% were RF-IgM positive. There were 108 (65%) patients who were both anti-CCP and RF positive, 20 patients were RF positive and anti-CCP negative and 4 patients were anti-CCP positive and RF negative. At enrollment, the average disease duration was 14 ($\pm$ 7) months, there were 78% patients receiving DMARD therapy, and the average BMI was 32.1 ($\pm$ 7.6) kg/m².

Patient characteristics and demographics at enrollment are summarized in Table 1. Of patients included in the analysis, 39% reported that they had never consumed alcohol and 61% either currently consumed alcohol or consumed alcohol in the past. Alcohol consumers were more likely to report a history of cigarette smoking ($p < 0.001$) but were similar to non-alcohol consumers in age, sex, and other demographics. DMARD therapy was similar in alcohol consumers and non-alcohol consumers ($p = 0.961$). Likewise, methotrexate use was similar between alcohol consumers and non-alcohol consumers ($p = 0.449$) and was similar in those consuming ≥ 15 alcoholic beverages per month to those consuming < 15 per month ($p = 0.735$). There were 5 patients on methotrexate plus biologic combination therapy and 18 patients on methotrexate plus hydroxychloroquine combination therapy. There was no significant difference between alcohol consumers and non-alcohol consumers on any type of methotrexate plus DMARD combination therapy ($p = 0.775$).

In those patients that consumed alcohol, 74 reported that they had, on average, less than 15 (mean = 4.24 ± 3.61 , range 1-12) alcoholic beverages per month and 27 reported that they had ≥ 15 (mean = 66.61 ± 68.71 , range 15-330) alcoholic beverages per month. The group consuming ≥ 15 alcoholic beverages per month had the highest SHS at baseline (mean 4.53 ± 7.31) and at the follow-up visit (mean 6.52 ± 10.86). SHS progression associated with monthly alcohol consumption is shown graphically in Figure 1. The checkmark shaped graph shows that each additional alcoholic beverage consumed from 0-14 beverages is associated with an increasingly lower SHS change from baseline to follow-up. The trend reverses with each additional alcoholic beverage ≥ 15 increasing the SHS change from baseline to follow-up.

Associations of SHS with covariates in both univariate and multivariate analyses are summarized in Table 2. In the univariate analysis, education level was a significant predictor of SHS progression during the first three years of RA. Compared to those without a high school education, those with a bachelor's degree had the least progression ($p = 0.001$), followed by those with a high school education and possibly some college ($p = 0.030$). Increased BMI was associated with significantly less SHS progression ($p < 0.001$) as was the use of DMARD therapy at enrollment ($p < 0.001$). Covariates associated with elevated SHS progression during the first three years of RA included anti-CCP antibody positivity ($p < 0.001$), IgM-RF positivity ($p < 0.001$), pain level ($p < 0.001$) and the time lapse between the baseline visit and the three-year follow-up visit ($p < 0.001$). SHS progression was not associated with age, disease duration at enrollment, sex, income, HLA-DRB1 SE, CRP, or smoking status. There was a non-significant trend in unadjusted analyses of SHS progression per alcoholic beverage consumed (per month) in individuals consuming ≥ 15 alcoholic beverages per month ($p = 0.075$) though not in those consuming < 15 beverages per month ($p = 0.931$).

In the multivariate analysis, higher education level and DMARD therapy retained their protective effect while BMI did not (Table 2). Anti-CCP antibody positivity, IgM-RF positivity, and the time lapse between the baseline visit and the three-year follow-up visit remained significantly associated with SHS progression. Pain was excluded from the analysis as described previously; results for all other covariates were similar to those observed in univariate analysis. Among those consuming more than 15 alcoholic beverages

per month, each additional beverage consumed was associated with a mean progression in SHS of 0.007 units (95% CI: 0.001-0.013, $p = 0.017$). This was not apparent in those consuming fewer than 15 alcoholic beverages per month, where there was a non-significant mean change in SHS progression of -0.005 units (95% CI: -0.041 - 0.031 , $p = 0.802$). A single outlier was identified with an average consumption of 330 beverages per month. The analysis was repeated after removing the outlier and the outcomes did not differ (data not shown).

Discussion

In the present study we investigated the associations of alcohol in RA course using radiographic joint damage as the primary indicator of disease progression during the early stages of RA. To our knowledge, this is the first study to evaluate such associations in an African American cohort. Our findings suggest that individuals consuming greater than 15 alcoholic beverages per month have significantly worse rates of radiographic disease progression with each additional alcoholic beverage consumed. This association was not evident in those consuming fewer than 15 beverages per month. The results therefore appear to reflect a somewhat paradoxical dose-dependent effect of alcohol in the natural course of RA. In the low consumption group, each additional alcoholic beverage per month has an increasingly more pronounced protective effect (albeit not statistically significant) until the fifteenth beverage is reached at which point each additional beverage has an increasingly more severe rate of radiographic disease progression. Our results indicate that there might be a “checkmark-shaped” relationship with alcohol consumption and disease progression as depicted in Figure 1.

This apparent paradoxical dose-dependent effect of alcohol coincides with findings from the Swiss Clinical Quality Management Project in Rheumatoid Arthritis.(12) These investigators found that the rate of radiographic progression after four years of follow up, compared with non-drinkers, was significantly less severe in occasional drinkers and daily drinkers but more severe in heavy alcohol drinkers. Although our results did not indicate a significant reduction in the rate of disease progression in the low consumption group, they did trend in that direction. These slight differences might have arisen because we adjusted for BMI. In our cohort BMI was not significantly associated with disease progression but trended towards having a protective effect. This is similar to others studies who have found that BMI has a robustly protective effect on radiographic disease progression.(27-31) If we had not adjusted for this it may have falsely shifted our results away from the null and incorrectly elevated our effect size.

Not all of the studies investigating RA disease progression have found worse disease in high alcohol consumption groups. A European case-control study demonstrated that radiographic disease severity was inversely associated with higher levels of alcohol consumption, but it is important to note that this was a cross-sectional component of the analysis.(3) It is possible that our results differed from these primarily because our study design allowed us to follow disease progression longitudinally over multiple visits. Furthermore, the cut-offs for high alcohol consumption between studies differed. In the European group, the highest alcohol consumption group included everyone who consumed > 10 beverages per month. In our

cohort use of this cut-off would have potentially missed the stark change in the direction of disease progression we found in those consuming more than 15 beverages per month. By including individuals from both the unexposed group (i.e., < 15 beverages per month) and the exposed group (i.e., ≥ 15 beverages per month) we found that there may be a threshold limit approximating 15 alcoholic beverages per month where the adverse effects of alcohol may begin to accumulate and cause worsening degrees of disease progression in patients with RA.

Our results potentially coincide with previously reported biological effects of alcohol. Levels of circulating TNF- α are elevated in chronic alcoholics, presumably heavy drinkers, due to increased cellular expression of toll-like receptors.(9) Likewise, IL-6 is elevated with moderate-to-high alcohol consumption but appears to be reduced with low alcohol consumption ($p = 0.005$).⁽³²⁾ Binge drinking also significantly increases the levels of IL-6 in mice ($p < 0.05$).⁽³³⁾ The relationship between these cytokines and differing levels of alcohol consumption might help explain our dose-dependent observation and offer some explanation as to why there was an increase in radiographic progression in our high alcohol consumption group but none in our low consumption group. The underlying mechanisms involved are still under investigation, but one theory suggests that IL-6, and TNF- α (increased with high levels of alcohol intake) may promote osteoclastogenesis. This is thought to lead to pathological bone resorption and more severe RA disease activity.⁽³⁴⁻³⁸⁾ Additionally, IL-6 and TNF- α have been shown to promote synovitis through the recruitment of inflammatory cells and synovial fibroblast proliferation.⁽³⁸⁾ Although the biologic mechanisms were not the primary focus of this study, higher levels of CRP were evident, although not reaching statistical significance, in those with a history of alcohol consumption versus those without. Because CRP is a downstream inflammatory marker of IL-6 (38), the biologic mechanisms are plausible and should be investigated further.

Although radiographic data in this study was collected longitudinally, our study was limited in that patients' history of alcohol consumption was only collected at baseline. This limits our ability to conclude whether or not our patients' disease progression was associated with prior alcohol use or current alcohol use. Additional limitations to our study include the potential for misclassification bias because alcohol use might be underreported and because our questionnaire did not specify the quantity of alcohol per beverage. Although these were potential sources of error we believe that this would only bias our results towards the null suggesting that the effects observed in our study represent conservative risk estimates. Channelling may also be a source of bias if alcohol use were to preclude being on DMARD therapy but this is unlikely since no differences in DMARD use or methotrexate use were identified based on different levels of alcohol consumption reported. Lastly, even though potential confounders were controlled for in our analysis, it is possible that residual confounding remains as the categorizations used may be oversimplified and because of the limited capacity to completely encompass confounders such as socioeconomic status which may influence alcohol intake and disease progression. Despite these limitations there are several notable strengths with our study. To our knowledge, this is the first study to evaluate the effects of alcohol use on radiographic disease progression in North America. Furthermore, this is the first study to look at these associations in an entirely African American cohort; a traditionally understudied group.

In summary, we found a dose-dependent relationship between alcohol use and radiographic disease progression in RA. Individuals who consume 15 or more alcoholic beverages per month have accelerated rates of radiographic joint damage. In addition to extending our findings into other populations, further work should focus on disease outcomes associated with alcohol cessation in individuals who consume large amounts of alcohol.

Acknowledgments

The authors would also like to thank the CLEAR registry coordinators and many patients for their participation in this effort.

Support: Mr. Davis' effort was supported by the University of Nebraska Medical Center Enhanced Medical Education Tract. Dr. Mikuls' work was supported by the Nebraska Arthritis Outcomes Research Center, the American College of Rheumatology, and the Veterans Affairs Office of Research & Development (VA Merit). The CLEAR Registry (PI, Dr. Bridges) is also supported by NIH grant 2P60 AR048095 UAB Multidisciplinary Clinical Research Center.

References

1. Mikuls TR, Levan T, Gould KA, Yu F, Thiele GM, Bynote KK, et al. Impact of interactions of cigarette smoking with NAT2 polymorphisms on rheumatoid arthritis risk in African Americans. *Arthritis Rheum.* 2012; 64(3):655–64. [PubMed: 21989592]
2. Mikuls TR, Sayles H, Yu F, Levan T, Gould KA, Thiele GM, et al. Associations of cigarette smoking with rheumatoid arthritis in African Americans. *Arthritis Rheum.* 2010; 62(12):3560–8. [PubMed: 20722010]
3. Maxwell JR, Gowers IR, Moore DJ, Wilson AG. Alcohol consumption is inversely associated with risk and severity of rheumatoid arthritis. *Rheumatology (Oxford).* 2010; 49(11):2140–6. [PubMed: 20667949]
4. Källberg H, Jacobsen S, Bengtsson C, Pedersen M, Padyukov L, Garred P, et al. Alcohol consumption is associated with decreased risk of rheumatoid arthritis: results from two Scandinavian case-control studies. *Ann Rheum Dis.* 2009; 68(2):222–7. [PubMed: 18535114]
5. Pedersen M, Jacobsen S, Klarlund M, Pedersen BV, Wiik A, Wohlfahrt J, et al. Environmental risk factors differ between rheumatoid arthritis with and without auto-antibodies against cyclic citrullinated peptides. *Arthritis Res Ther.* 2006; 8(4):R133. [PubMed: 16872514]
6. Cerhan JR, Saag KG, Criswell LA, Merlino LA, Mikuls TR. Blood transfusion, alcohol use, and anthropometric risk factors for rheumatoid arthritis in older women. *J Rheumatol.* 2002; 29(2):246–54. [PubMed: 11838841]
7. Nelson S, Bagby GJ, Bainton BG, Summer WR. The effects of acute and chronic alcoholism on tumor necrosis factor and the inflammatory response. *J Infect Dis.* 1989; 160(3):422–9. [PubMed: 2668425]
8. Imhof A, Koenig W. Alcohol inflammation and coronary heart disease. *Addict Bio.* 2003; 8(3):271–7. [PubMed: 13129828]
9. Mandrekar P, Szabo G. Signalling pathways in alcohol-induced liver inflammation. *J Hepatol.* 2009; 50(6):1258–66. [PubMed: 19398236]
10. Vidali M, Hietala J, Occhino G, Ivaldi A, Sutti S, Niemelä O, et al. Immune responses against oxidative stress-derived antigens are associated with increased circulating tumor necrosis factor- α in heavy drinkers. *Free Radic Biol Med.* 2008; 45(3):306–11. [PubMed: 18460346]
11. Poullis A. Alcohol, obesity, and TNF- α Reply. *Gut.* 2001; 49(2):313–4. [PubMed: 11476082]
12. Nissen MJ, Gabay C, Scherer A, Finckh A. The effect of alcohol on radiographic progression in rheumatoid arthritis. *Arthritis Rheum.* 2010; 62(5):1265–72. [PubMed: 20213811]
13. Fuchs FD, Chambless LE. Is the cardioprotective effect of alcohol real? *Alcohol.* 2007; 41(6):399–402. [PubMed: 17936508]

14. Sacco RL, Elkind M, Boden-Albala B, Lin IF, Kargman DE, Hauser WA, et al. The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA*. 1999; 281(1):53–60. [PubMed: 9892451]
15. Sempos CT, Rehm J, Wu T, Crespo CJ, Trevisan M. Average volume of alcohol consumption and all-cause mortality in African Americans: the NHEFS cohort. *Alcohol Clin Exp Res*. 2003; 27(1): 88–92. [PubMed: 12544011]
16. Rehm J, Sempos CT. Alcohol consumption and all-cause mortality. *Addiction*. 1995; 90(4):471–80. [PubMed: 7773106]
17. Kerr WC, Greenfield TK, Bond J, Ye Y, Rehm J. Racial and ethnic differences in all-cause mortality risk according to alcohol consumption patterns in the national alcohol surveys. *Am J Epidemiol*. 2011; 174(7):769–78. [PubMed: 21856649]
18. Bridges SL, Hughes LB, Mikuls TR, Howard G, Tiwari HK, Alarcón GS, et al. Early rheumatoid arthritis in African-Americans: the CLEAR Registry. *Clin Exp Rheumatol*. 2003; 21(5 Suppl 31):S138–45. [PubMed: 14969066]
19. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum*. 1988; 31(3):315–24. [PubMed: 3358796]
20. Van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. *J Rheumatol*. 1999; 26(3):743–5. [PubMed: 10090194]
21. Bridges SL, Causey ZL, Burgos PI, Huynh BQN, Hughes LB, Danila MI, et al. Radiographic severity of rheumatoid arthritis in African Americans: results from a multicenter observational study. *Arthritis Care Res (Hoboken)*. 2010; 62(5):624–31. [PubMed: 20461784]
22. Hughes LB, Morrison D, Kelley JM, Padilla MA, Vaughan LK, Westfall AO, et al. The HLA-DRB1 shared epitope is associated with susceptibility to rheumatoid arthritis in African Americans through European genetic admixture. *Arthritis Rheum*. 2008; 58(2):349–58. [PubMed: 18240241]
23. Mikuls TR, Holers VM, Parrish L, Kuhn KA, Conn DL, Gilkeson G, et al. Anti-cyclic citrullinated peptide antibody and rheumatoid factor isotypes in African Americans with early rheumatoid arthritis. *Arthritis Rheum*. 2006; 54(9):3057–9. [PubMed: 16948136]
24. Mikuls TR, LeVan TD, Sayles H, Yu F, Caplan L, Cannon GW, et al. Soluble CD14 and CD14 polymorphisms in rheumatoid arthritis. *J Rheumatol*. 2011; 38(12):2509–16. [PubMed: 21921097]
25. Hardin, J.; Hilbe, J. Generalized estimating equations. Chapman & Hall/CRC; Boca Raton, FL: 2003.
26. Zhang J, Redden DT, McGwin G, Callahan LF, Smith EA, Alarcón GS, et al. Generalized bone loss as a predictor of three-year radiographic damage in African American patients with recent-onset rheumatoid arthritis. *Arthritis Rheum*. 2010; 62(8):2219–26. [PubMed: 20506234]
27. Westhoff G, Rau R, Zink A. Radiographic joint damage in early rheumatoid arthritis is highly dependent on body mass index. *Arthritis Rheum*. 2007; 56(11):3575–82. [PubMed: 17968909]
28. Van der Helm-van Mil AHM, Van der Kooij SM, Allaart CF, Toes REM, Huizinga TWJ. A high body mass index has a protective effect on the amount of joint destruction in small joints in early rheumatoid arthritis. *Ann Rheum Dis*. 2008; 67(6):769–74. [PubMed: 17965124]
29. Kaufmann J, Kielstein V, Kilian S, Stein G, Hein G. Relation between body mass index and radiological progression in patients with rheumatoid arthritis. *J Rheumatol*. 2003; 30(11):2350–5. [PubMed: 14677176]
30. Stavropoulos-Kalinoglou A, Metsios GS, Koutedakis Y, Kitas GD. Obesity in rheumatoid arthritis. *Rheumatology (Oxford)*. 2011; 50(3):450–62. [PubMed: 20959355]
31. Wolfe F, Michaud K. Effect of body mass index on mortality and clinical status in rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2012; 64(10):1471–9. [PubMed: 22514152]
32. Lu B, Solomon DH, Costenbader KH, Keenan BT, Chibnik LB, Karlson EW. Alcohol consumption and markers of inflammation in women with preclinical rheumatoid arthritis. *Arthritis Rheum*. 2010; 62(12):3554–9. [PubMed: 20827783]
33. Callaci JJ, Himes R, Lauing K, Wezeman FH, Brownson K. Binge alcohol-induced bone damage is accompanied by differential expression of bone remodeling-related genes in rat vertebral bone. *Calcif Tissue Int*. 2009; 84(6):474–84. [PubMed: 19330277]

34. Boyce BF, Schwarz EM, Xing L. Osteoclast precursors: cytokine-stimulated immunomodulators of inflammatory bone disease. *Curr Opin Rheumatol.* 2006; 18(4):427–32. [PubMed: 16763465]
35. Teitelbaum SL. Osteoclasts; culprits in inflammatory osteolysis. *Arthritis Res Ther.* 2006; 8(1): 201. [PubMed: 16356195]
36. Zhao B, Grimes SN, Li S, Hu X, Ivashkiv LB. TNF-induced osteoclastogenesis and inflammatory bone resorption are inhibited by transcription factor RBP-J. *J Exp Med.* 2012; 209(2):319–34. [PubMed: 22249448]
37. Schett G, Teitelbaum SL. Osteoclasts and Arthritis. *J Bone Miner Res.* 2009; 24(7):1142–6.
38. Hashizume M, Mihara M. The roles of interleukin-6 in the pathogenesis of rheumatoid arthritis. *Arthritis.* 2011; 2011:765624. [PubMed: 22046525]

Figure 1.

Radiographic disease progression, from baseline to a second time point 3 years from disease onset, as measured by modified Sharp/van der Heijde score (SHS progression) is summarized based on the average number of alcoholic beverages consumed per month. An inflection point occurs at 15 alcoholic beverages per month. Each alcoholic beverage consumed, on average, below 15 drinks per month has an progressively lower SHS change from baseline to follow-up while each beverage consumed > 15 beverages per month has a progressively higher SHS change.

Table 1

Patient demographics at baseline in African American patients with rheumatoid arthritis (N = 166)

	Alcohol Use		p-value
	Never (n=65)	Past/Current (n=101)	
Mean, age (years) [†]	50.44	52.14	0.398
Mean, disease duration (months) [†]	14.20	14.62	0.717
Sex: female, %	90.8	82.2	0.124
Mean, BMI (kg/m²) [†]	32.55	31.81	0.540
Completed Education: [†]			
<i>No high school degree, %</i>	21.5	34.6	0.495
<i>High school +/- some college, %</i>	67.7	48.5	
<i>Bachelor's Degree or higher, n %</i>	10.8	16.8	
Income: [†]			
< \$5,000, %	9.2	8.9	0.795
\$5,000 – \$9,999, %	13.8	21.8	
\$10,000 – \$14,999, %	12.3	9.9	
\$15,000 – \$19,999, %	16.9	8.9	
\$20,000 – \$29,999, %	12.3	17.8	
\$30,000 – \$49,999, %	15.4	16.8	
\$50,000 – \$99,999, %	20.0	10.9	
>\$100,000, %	0.0	2.0	
Unknown, %	0.0	3.0	
Smoking Status			
<i>Never, %</i>	69.3	32.7	< 0.001
<i>Former, %</i>	16.9	33.7	
<i>Current, %</i>	13.8	33.7	
Current DMARD Therapy: [†]			
<i>Biologic agents, % *</i>	3.1	4.9	0.961
<i>Hydroxychloroquine, % [‡]</i>	10.8	14.8	
<i>Methotrexate, % [†]</i>	44.6	38.6	
<i>Other DMARDs, % **</i>	4.6	4.9	
<i>Combination therapy, %</i>	15.4	13.9	
<i>Not on therapy, %</i>	21.5	22.8	
HLA-DRB1 Shared Epitope			
<i>Present, n (%)</i>	47.7	46.5	0.884
Anti-CCP antibody			
<i>Positive, n (%)</i>	72.3	64.4	0.286
Rheumatoid Factor IgM status			
<i>Positive, n (%)</i>	76.9	77.2	0.964
Mean, C-Reactive Protein (mg/L)	18.66	28.39	0.090

* Biologics – Anakinra, Infliximab, etanercept

** Other DMARDs – gold, penicillamine, sulfasalazine, leflunomide, azathioprine, cyclosporine, cyclophosphamide

[†] Analysis of variance was used to compare means

[‡] Monotherapy only

Table 2

Association of modified Sharp/van der Heijde Score (SHS) during the first 3 years of rheumatoid arthritis and alcoholic beverage consumption at baseline in 166 African American patients. Results from generalized estimating equations model.

Variable	SHS - Univariate Analysis			SHS - Multivariate Analysis		
	Beta Coefficient (95% CI)	Z score	P value	Beta Coefficient (95% CI)	Z score	P value
Alcoholic beverages, per beverage consumed						
< 15 per month (n = 139)	−0.001 (−0.032, 0.029)	−0.09	0.931	−0.005 (−0.041, 0.031)	−0.25	0.802
15 per month (n = 27)	0.004 (0.000, 0.009)	1.78	0.075	0.007 (0.001, 0.013)	2.39	0.017
Age †	0.002 (−0.010, 0.014)	0.33	0.744	0.013 (0.000, 0.027)	1.90	0.058
Disease duration at enrollment † (months)	0.017 (−0.004, 0.037)	1.56	0.118	0.021 (−0.002, 0.044)	1.81	0.070
Time lapse between visits	0.346(0.277, 0.415)	9.84	<0.001	0.335(0.251, 0.419)	7.83	<0.001
Sex †						
Female	−0.286 (−0.704, 0.133)	−1.34	0.181	0.053 (−0.451, 0.559)	0.21	0.838
Education						
No HS degree	Ref			Ref		
HS degree +/- some college	−0.367 (−0.697, −0.036)	−2.17	0.030	−0.533 (−0.904, −0.162)	−2.81	0.005
Bachelors degree or higher	−0.826 (−1.316, −0.335)	−3.30	0.001	−0.714 (−1.253, −0.180)	−2.60	0.009
Income	0.009 (−0.064, 0.081)	0.23	0.817	–	–	–
BMI (kg/m ²) ‡	−0.039 (−0.060, −0.019)	−3.79	<0.001	−0.023 (−0.046, 0.000)	−1.94	0.053
Current DMARD Therapy * ‡	−0.771 (−1.131, −0.410)	−4.19	<0.001	−0.682 (−1.058, −0.306)	−3.56	<0.001
Anti-CCP positivity ‡	1.011(0.667, 1.355)	5.76	<0.001	0.677(0.210, 1.144)	2.84	0.004
IgM-RF positivity ‡	1.044 (0.656, 1.432)	5.28	<0.001	0.574(0.028, 1.119)	2.06	0.039
HLA-DRB1 Shared Epitope	−0.140 (−0.443, 0.162)	−0.91	0.364	–	–	–
C-Reactive Protein	0.004 (0.000, 0.008)	1.82	0.069	−0.001 (−0.006, 0.004)	−0.34	0.735
Pain VAS ‡	0.096(0.042, 0.150)	3.50	<0.001	–	–	–
Smoking Status						
Never	Ref			Ref		
Former	−0.358 (−0.732, 0.016)	−1.88	0.060	−0.175 (−0.617, 0.266)	−0.78	0.436
Current	0.156 (−0.211, 0.523)	0.83	0.406	0.125 (−0.302, 0.552)	0.57	0.567

* DMARD therapy included anakinra, infliximab, etanercept, gold, penicillamine, sulfasalazine, leflunomide, azathioprine, cyclosporine, cyclophosphamide

† Age, disease duration, and sex forced into multivariate model

‡ Body Mass Index (BMI), Disease-Modifying Antirheumatic drug (DMARD), Anti-cyclic Citrullinated Peptide (Anti-CCP), IgM-Rheumatoid Factor (RF), Visual Analogue Scale (VAS)