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Use of Hydroxychloroquine is Associated with Improved Lipid Profile in Rheumatoid Arthritis Patients

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Abstract

Background/Purpose—We examined the association between hydroxychloroquine (HCQ) and plasma lipid and glucose levels in RA cohort.

Patients and Methods—We performed compared fasting lipid profiles and plasma glucose between patients that were and were not taking HCQ. We divided patients into three groups based on HCQ exposure during follow up : Those who had never taken HCQ, those who took it intermittently, and those who took it continuously. We used multivariable models and propensity scoring to compensate for the effect of non-random treatment assignment.

Results—We followed 1261 RA patients for a total of 4,605 observations between 1996 and 2014. After adjusting for age, sex, ethnicity, other DMARD, lipid lowering medications, bmi, and smoking, patients taking HCQ at baseline had significantly lower total cholesterol (TC) (P 0.001), LDL (P 0.001), triglycerides (TG) (P =0.013), and lipid profile ratios TC/HDL (P 0.001) and LDL/HDL (P 0.001), as well as higher HDL (P 0.001).

In longitudinal analyses, after adjusting for confounders patients that continuously took HCQ showed significantly lower TC, LDL, TC/HDL, LDL/HDL, and higher HDL (P 0.01). Fasting plasma glucose levels were not significantly associated with HCQ exposure.

Conclusion—HCQ use was associated with lower lipid levels but not with the plasma glucose in this RA cohort. These findings support the need for a randomized trial to establish the role of HCQ in cardiovascular disease prevention in RA patients.

Keywords

rheumatoid arthritis; hydroxychloroquine; lipids; glucose

Introduction

Rheumatoid arthritis (RA) is a chronic disease characterized by systemic inflammation that leads to joint damage and disability, and may be associated with increased risk of

cardiovascular disease (CVD) a major cause of morbidity and mortality in RA. [1] The relationship between RA disease activity, lipid levels and cardiovascular diseases is complex [2, 3] However, CVD risk factor modification, such as reducing total cholesterol and plasma glucose may be beneficial for preventing CVD. Hydroxychloroquine (HCQ), a disease modifying anti rheumatic drug (DMARD) with a good safety profile and low cost, has been reported to improve lipid profiles [4–6] and glucose level in RA. [7, 8] We aimed to examine the association between the use of HCQ and plasma lipid and glucose levels in a large RA cohort.

Patients and Methods

From 1996 to 2009, we recruited 1328 consecutive patients who met the 1987 criteria for RA[9] from private and public rheumatology clinics in San Antonio, Texas. We have described this cohort in previous publications.[10–12] All patients participated in a comprehensive baseline evaluation of their clinical and psychosocial characteristics conducted by a physician and trained research assistants. We followed patients prospectively for yearly follow up evaluations in which we assessed clinical features of RA, laboratory measures, as well as DMARD use. The study protocol was approved by our IRB, and all patients provided signed, informed consent.

Variables

Demographic information included age, sex, ethnicity and duration of RA. The duration of RA was considered to be the time between RA diagnosis and the evaluation date. For clinical purpose we include prednisone use, tender, swollen and deformed joint counts, disease activity score (DAS28ESR), and hand sharp score. [13, 14]

Laboratory Studies

The erythrocyte sedimentation rate (ESR) was measured by the Westergren technique. Total plasma cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL), and glucose were measured using a Synchron LX automated system (Beckman Coulter, Fullerton, CA). Patients were asked to fast overnight before laboratory testing.

Statistical analysis

We performed cross sectional analyses comparing fasting lipid profiles and plasma glucose between patients that were and were not taking HCQ at baseline. We subsequently divided patients into three groups based on HCQ exposure: Those who did not take HCQ during the time of our study, those who took it intermittently, and those who took it continuously throughout the study. Using these groups, we performed generalized estimated equation (GEE) regression models including all follow up visits to examine plasma lipid and glucose levels by HCQ exposure. We adjusted for age, sex, duration of RA, ethnicity, use of lipid lowering medications, anti-TNF alpha medications and other non-biologic DMARDs including methotrexate, sulfasalazine, leflunomide, azathioprine, and diabetes medication. We also compare visits with and without HCQ, using the GEE regression model. In an alternative approach to account for potential confounding by indication, we estimated the patient's propensity to receive HCQ and use the propensity score as a covariate in regression

model. The propensity score was the predicted probability that a patient would be taking HCQ at a given visit, which was calculated from a logistic regression model using the independent variables listed in tables 1 –3.

Results

A total of 1328 patients were recruited into the study. However, 67 lacked complete lipid profiles, so our final sample included 1261 patients (938 female, 323 male) with a mean $\pm$ SD age of 59.6 ± 11.5 years. At baseline, 254 patients were on HCQ and 1007 were not. After adjusting for age, sex, ethnicity, lipid lowering medications, bmi, smoking and use of any other DMARDs, patients taking HCQ had significantly lower TC ($p = 0.001$), LDL ($p < 0.001$), TG ($p = 0.009$), and lipid profile ratios TC/HDL ($p < 0.001$) and LDL/HDL ($p < 0.001$) compared to those who were not taking HCQ. Furthermore, HDL was significantly higher in patients taking HCQ ($p < 0.001$). Plasma glucose level was not significantly associated with HCQ use ($p = 0.2$). Patients taking HCQ at baseline also had significantly lower ESR ($p = 0.042$), though this association lost statistical significance after the adjustment of other DMARD use ($p = 0.1$).

With respect to clinical analysis including prednisone use, swollen, tender joints, DAS28 ESR, and Sharp score, there were no statistically significant differences between those who were currently taking HCQ versus those who were not, except for DAS28 ESR and any other DMARD (Table 1).

When taking into account follow-up visits, we divided patients based on HCQ exposure: those who had never taken HCQ during the time of our study (used as referent group), those who took it intermittently, and those who took it continuously throughout their time in the study. After adjusting for confounders, the patients who had never taken HCQ had significantly higher TC ($p = 0.03$, $p = 0.01$), LDL ($p = 0.03$, $p < 0.001$), TG ($p < 0.01$, $p < 0.01$) and lipid profile ratios TC/HDL ($p = 0.001$, $p < 0.001$) and LDL/HDL ($p = 0.04$, $p < 0.001$) when compared to those who took the drug intermittently or continuously, respectively. HDL was significantly higher in patients who took HCQ continuously versus those who have never taken it ($p < 0.001$). HCQ use was associated with lower plasma glucose concentration, but the difference was not significant after adjusting for the propensity score, (Table 2). Patients who had never taken HCQ had significantly higher ESR compared to those who took it continuously throughout the study ($p = 0.04$), though there was no significant difference when compared to those who took the drug intermittently (Table 2). In all models, compared to patients with no HCQ exposure, patients taking HCQ continuously showed a more significant improvement in lipid profiles, glucose and ESR than those who took it intermittently.

We found the following average differences in lipids comparing the never exposed versus continuously exposed group in the pooled follow up visits: LDL decrease of 9.3 mg/dl ($p < 0.001$), TG decrease 16.8 mg/dl ($p < 0.001$), TC decrease 4.7 mg/dl ($p < 0.01$), HDL increase 7.8 mg/dl ($p < 0.001$), LDL/HDL decrease 0.45 ($p < 0.001$), and TC/HDL decrease 0.59 ($p < 0.001$).

When we compare follow up visits of patients with and without HCQ treatment, we found also statistically significant differences in all lipids level ($p < 0.0001$). Table 3.

With respect to clinical findings, swollen joints, DAS 28 ESR and Sharp Score were less severe in the group who take continuously HCQ versus those who never took HCQ ($p < 0.01$) and deformed joints and sharp score were also significantly different in the intermittently taken HCQ group compared to those who had never taken it ($p = 0.01$) (Table 2).

We tested a HCQ X ethnic group interaction in the models for lipids measurements and it was not significant. This finding suggests that the effect of HCQ does not vary between ethnic groups.

Discussion

Despite recent advances in medical treatment, high cholesterol remains a significant public health problem in the United States, with more than one-quarter of adults aged 40–74 having high LDL-cholesterol.[15] Increased risk in CVD morbidity and mortality have been described in RA patients, independent of traditional risk factor like hypertension, diabetes, hyperlipidemia, smoking or increased age. [16, 17]

Our results suggest that HCQ is associated with significant lower in TC, TG, and LDL, as well as a significant increase in HDL in RA patients. These findings are particularly important because RA patients are predisposed to CVD.

In 1997, a prospective randomized clinical trial comparing the effect of intramuscular (IM) gold and HCQ on lipid profiles of RA patients suggested that HCQ has beneficial effects on lipids. Patients in the HCQ group had significantly higher HDL and lower TC compared to the IM gold group. In a cohort of 706 RA patients, Morris et al demonstrated that use of HCQ was associated with a significant decrease in LDL of 7.55mg/dl, decrease in TC of 7.70 mg/dl, decrease in LDL/HDL of 0.136, and decrease in TC/HDL of 0.191, with a non-significant increase of 1.02mg/dl in HDL. Similarly, we found a significantly lower average LDL, TG, TC, LDL/HDL and TC/HDL, as well as a significant increase in HDL in patients taking HCQ. However, the average differences were greater or similar in our cohort with respect to LDL, LDL/HDL, TG and TC/HDL. The significant increase in HDL is important to note because HDL is considered a powerful predictive tool, independent of other known coronary heart disease risk factors among postmenopausal women.[18] In another study of 155 women with RA or SLE was found an association between HCQ treatment and low serum level of TC, LDL, and TG level, but with no increased level of HDL.[6] In a more recent and smaller study of 72 lupus patients following for two year levels of TC, TG, LDL and HDL were significantly improved after treatment with HCQ.[19]

Similar findings, showing the benefit of HCQ as a lipid lowering medication, have been shown in systemic lupus erythematosus patients. [6, 15, 19–22]

In a cross sectional study, Urowitz et al [23] studied 123 patients with lupus and found that TC, VLDL, and LDL levels were significantly lower in patients taking antimalarial

including patients taking concomitant prednisone. The cholesterol lowering effect of HCQ was found more pronounced in those SLE patients who are in stable doses of steroid or those who are initiating treatment with steroids.[24] However, in our cohort we didn't find any differences when comparing HCQ in patients taking or not taking corticosteroids, probably because the prednisone use was similar in patients taking HCQ and those who were not taking it.

Considering that patients with RA have more difficulty in achieving a goal LDL when treated with statins compared to the general population, [25] HCQ is a reasonable and inexpensive adjuvant alternative to control the high TC or LDL level. Although the absolute differences in lipids level are not great, the statistical significance is high. Considering that small decrease in lipids level may be a protective factor in major cardiovascular disease, especially in secondary prevention, the differences that we found may still have clinical relevance.

The exact mechanism by which HCQ can lower plasma lipid levels is still unknown. It has been reported that chloroquine, which is related to HCQ, is a potent inhibitor of cholesterol biosynthesis by isolated rat hepatocytes, [26] and may increase LDL receptors, activity of HMG-Co reductase, and slow degradation of this enzyme. [27] The beneficial effect on glucose metabolism may also play an important role in decreasing lipid level. [28] In addition to lowering cholesterol, HCQ may improve plasma glucose levels. Insulin resistance is highly prevalent in RA patients and this condition may play an important role in subclinical atherosclerosis. [29] Although not all studies confirm that HCQ improve the sensitivity to insulin, [30] others have shown improvement in insulin sensitivity, and a decrease in TC and TG level.[31]

The glucose lowering efficacy, responsiveness, duration of action and impact on quality-of-life of HCQ, when added as an anti-hyperglycemic agent to patients with sulfonylurea-refractory type 2 diabetes was demonstrated in a study with 135 obese patients with type 2 diabetes, especially in those with glycosylated hemoglobin <13.5%. [32] In our study, we found no difference in the plasma glucose level at baseline and the difference during the follow up visits was not significant after adjusting for confounding.

Our study addressing HCQ as a lipid lowering medication in RA patients has strengths and limitations. Among its strengths, our cohort is large enough to provide the power to detect small effects. It is a prospective observational study in which a rheumatologist examined the patients, systematically asking questions about any medications that they were taking, and drawing blood for complete metabolic profile during each visit. We also have the benefit of a diverse cohort, recruited from a variety of health systems and socioeconomic strata. Furthermore, compared to patients taking HCQ, those who were not had similar ESR and DAS28ESR at baseline, thus decreasing the likelihood of an indication bias. We also used these data to score the patient's propensity to be receiving HCQ at each visit. These propensity scores, which were used as covariates in multivariable models, compensate for the effect of nonrandom treatment assignment. [33] The association of HCQ with lower lipid profile remained significant after adjustment for propensity score. One possible limitation is the fact that the recruitment period was quite long (1996–2009) during which there may

have been changes in the management of patients, beyond pharmacologically, but also in the delivery of service. There may have been changes in health care policy, which may have affected the outcomes we measured. Moreover, the pattern of use of HCQ regimen could have also changed over time.

Conclusion

HCQ use was associated with significantly lower TC, LDL, TG, and TC/HDL and LDL/HDL ratios, and with higher HDL. The association of HCQ with plasma glucose was not statistically significant after adjusting for confounding. Minimizing risk of CVD in RA patients remains a major concern in treating these patients. These findings suggest HCQ may help in reducing some traditional CV risk factors. Large randomized trials are needed to establish the potential of HCQ in CVD prevention in RA patients.

References

1. Wolfe F, Mitchell DM, Sibley JT, et al. The mortality of rheumatoid arthritis. *Arthritis Rheum.* 1994; 37:481–494. [PubMed: 8147925]
2. Lazarevic MB, Vitic J, Mladenovic V, et al. Dyslipoproteinemia in the course of active rheumatoid arthritis. *Semin Arthritis Rheum.* 1992; 22:172–178. [PubMed: 1295090]
3. Myasoedova E, Crowson CS, Kremers HM, et al. Lipid paradox in rheumatoid arthritis: the impact of serum lipid measures and systemic inflammation on the risk of cardiovascular disease. *Ann Rheum Dis.* 2011; 70:482–487. [PubMed: 21216812]
4. Morris SJ, Wasko MC, Antohe JL, et al. Hydroxychloroquine use associated with improvement in lipid profiles in rheumatoid arthritis patients. *Arthritis Care Res (Hoboken).* 2011; 63:530–534. [PubMed: 21452265]
5. Munro R, Morrison E, McDonald AG, et al. Effect of disease modifying agents on the lipid profiles of patients with rheumatoid arthritis. *Ann Rheum Dis.* 1997; 56:374–377. [PubMed: 9227167]
6. Wallace DJ, Metzger AL, Stecher VJ, et al. Cholesterol-lowering effect of hydroxychloroquine in patients with rheumatic disease: reversal of deleterious effects of steroids on lipids. *Am J Med.* 1990; 89:322–326. [PubMed: 2393036]
7. Penn SK, Kao AH, Schott LL, et al. Hydroxychloroquine and glycemia in women with rheumatoid arthritis and systemic lupus erythematosus. *J Rheumatol.* 2010; 37:1136–1142. [PubMed: 20436082]
8. Rekedal LR, Massarotti E, Garg R, et al. Changes in glycosylated hemoglobin after initiation of hydroxychloroquine or methotrexate treatment in diabetes patients with rheumatic diseases. *Arthritis Rheum.* 2010; 62:3569–3573. [PubMed: 20722019]
9. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum.* 1988; 31:315–324. [PubMed: 3358796]
10. Escalante A, del Rincon I. How much disability in rheumatoid arthritis is explained by rheumatoid arthritis? *Arthritis Rheum.* 1999; 42:1712–1721. [PubMed: 10446872]
11. Escalante A, Del Rincon I. The disablement process in rheumatoid arthritis. *Arthritis Rheum.* 2002; 47:333–342. [PubMed: 12115165]
12. Escalante A, del Rincon I, Mulrow CD. Symptoms of depression and psychological distress among Hispanics with rheumatoid arthritis. *Arthritis Care Res.* 2000; 13:156–167. [PubMed: 14635289]
13. Prevoo ML, van 't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum.* 1995; 38:44–48. [PubMed: 7818570]
14. Sharp JT, Young DY, Bluhm GB, et al. How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to assess rheumatoid arthritis? *Arthritis Rheum.* 1985; 28:1326–1335. [PubMed: 4084327]

15. Kuklina EV, Carroll MD, Shaw KM, Hirsch R. Trends in high LDL cholesterol, cholesterol-lowering medication use, and dietary saturated-fat intake: United States, 1976–2010. *NCHS Data Brief*. 2013;1–8.
16. del Rincon ID, Williams K, Stern MP, et al. High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. *Arthritis Rheum*. 2001; 44:2737–2745. [PubMed: 11762933]
17. del Rincon I, Freeman GL, Haas RW, et al. Relative contribution of cardiovascular risk factors and rheumatoid arthritis clinical manifestations to atherosclerosis. *Arthritis Rheum*. 2005; 52:3413–3423. [PubMed: 16255018]
18. Shai I, Rimm EB, Hankinson SE, et al. Multivariate assessment of lipid parameters as predictors of coronary heart disease among postmenopausal women: potential implications for clinical guidelines. *Circulation*. 2004; 110:2824–2830. [PubMed: 15492318]
19. Meng J, Lu Y, Dong X, Liu H. Long-term effects of hydroxychloroquine on metabolism of serum lipids and left ventricular structure and function in patients of systemic lupus erythematosus. *Zhonghua Yi Xue Za Zhi*. 2014; 94:965–968. [PubMed: 24851679]
20. Cairoli E, Rebella M, Danese N, et al. Hydroxychloroquine reduces low-density lipoprotein cholesterol levels in systemic lupus erythematosus: a longitudinal evaluation of the lipid-lowering effect. *Lupus*. 2012; 21:1178–1182. [PubMed: 22641182]
21. Kavanaugh A, Adams-Huet B, Jain R, et al. Hydroxychloroquine Effects on Lipoprotein Profiles (the HELP trial): A Double-Blind, Randomized, Placebo-Controlled, Pilot Study In Patients With Systemic Lupus Erythematosus. *J Clin Rheumatol*. 1997; 3:3–8. [PubMed: 19078110]
22. Marmor MF, Kellner U, Lai TY, et al. Revised recommendations on screening for chloroquine and hydroxychloroquine retinopathy. *Ophthalmology*. 2011; 118:415–422. [PubMed: 21292109]
23. Tam LS, Gladman DD, Hallett DC, et al. Effect of antimalarial agents on the fasting lipid profile in systemic lupus erythematosus. *J Rheumatol*. 2000; 27:2142–2145. [PubMed: 10990225]
24. Rahman P, Gladman DD, Urowitz MB, et al. The cholesterol lowering effect of antimalarial drugs is enhanced in patients with lupus taking corticosteroid drugs. *J Rheumatol*. 1999; 26:325–330. [PubMed: 9972966]
25. Myasoedova E, Gabriel SE, Green AB, et al. Impact of statin use on lipid levels in statin-naïve patients with rheumatoid arthritis versus non-rheumatoid arthritis subjects: results from a population-based study. *Arthritis Care Res (Hoboken)*. 2013; 65:1592–1599. [PubMed: 23592565]
26. Beynen AC, van der Molen AJ, Geelen MJ. Inhibition of hepatic cholesterol biosynthesis by chloroquine. *Lipids*. 1981; 16:472–474. [PubMed: 7266270]
27. Ben-Zvi I, Kivity S, Langevitz P, Shoenfeld Y. Hydroxychloroquine: from malaria to autoimmunity. *Clin Rev Allergy Immunol*. 2012; 42:145–153. [PubMed: 21221847]
28. Pareek A, Chandurkar N, Thomas N, et al. Efficacy and safety of hydroxychloroquine in the treatment of type 2 diabetes mellitus: a double blind, randomized comparison with pioglitazone. *Curr Med Res Opin*. 2014; 30:1257–1266. [PubMed: 24669876]
29. La Montagna G, Cacciapuoti F, Buono R, et al. Insulin resistance is an independent risk factor for atherosclerosis in rheumatoid arthritis. *Diab Vasc Dis Res*. 2007; 4:130–135. [PubMed: 17654447]
30. Solomon DH, Garg R, Lu B, et al. Effect of hydroxychloroquine on insulin sensitivity and lipid parameters in rheumatoid arthritis patients without diabetes mellitus: a randomized, blinded crossover trial. *Arthritis Care Res (Hoboken)*. 2014; 66:1246–1251. [PubMed: 24470436]
31. Araiza-Casillas R, Diaz-Molina R, Gonzalez-Ortiz M, Robinson-Navarro OM. Effects of hydroxychloroquine on insulin sensitivity and lipid profile in patients with rheumatoid arthritis. *Rev Med Chil*. 2013; 141:1019–1025. [PubMed: 24448858]
32. Gerstein HC, Thorpe KE, Taylor DW, Haynes RB. The effectiveness of hydroxychloroquine in patients with type 2 diabetes mellitus who are refractory to sulfonylureas—a randomized trial. *Diabetes Res Clin Pract*. 2002; 55:209–219. [PubMed: 11850097]
33. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998; 17:2265–2281. [PubMed: 9802183]

Table 1

Baseline characteristics of 1,261 RA patients by HCQ exposure.

	Currently taking HCQ (n=254)	Not Currently Taking HCQ (n=1,007)	P _{adj} [*]
Demographics			
Age, mean (SD)	57.2 (11.1)	57.4 (11.8)	0.8
Female, n (%)	200 (78%)	738 (73%)	0.07
Ethnic			0.6
Hispanic, n (%)	146(57)	598(59)	
White, n (%)	92 (36)	356 (35)	
Black n (%)	14(6)	37(4)	
Other, n (%)	2(1)	16(2)	
Duration of RA, years Mean ± SD	10.7 ± 9.0	12.2 ± 10.6	0.04
Laboratory			
Total Cholesterol mg/dl, mean (SD)	182.3 ± 35.6	190.5 ± 39.8	0.001
LDL mg/dl, mean ± SD	99.4 ± 30.6	109.3 ± 34.4	<0.001
HDL mg/dl, mean ± SD	58.3 ± 18.2	53.4 ± 16.0	<0.001
Triglycerides mg/dl, mean ± SD	123.6 ± 68.1	136.7 ± 79.4	0.009
Total Cholesterol/HDL, mean ± SD	3.4 ± 1.2	3.8 ± 1.5	<0.001
LDL/HDL, mean ± SD	1.9 ± 0.9	2.2 ± 1.1	<0.001
Plasma glucose mg/dl, mean ± SD	98.5 ± 36.6	102.6 ± 40.0	0.2
ESR mg/dl, mean ± SD ⁺⁺	26.1 ± 25.1	30.0 ± 25.7	0.1
Clinical			
Prednisone use, n(%)	101 (39.7)	392 (38.9)	0.5
Tender joints, mean(SD) ^{**}	8.2(8.5)	8.6(8.9)	0.5
Swollen joints, mean(SD) ^{**}	2.6(3.9)	3(4.5)	0.1
Deformed joints, mean(SD) ^{**}	6.73 (7.9)	6.97 (8.0)	0.23
DAS28ESR, mean(SD) ^{\$}	3.94 ± 1.67	4.20 ± 1.66	0.04
Sharp Score, mean (SD) [#]	60.6 ± 85.3	65.6 ± 86.3	0.4
Diabetes Med, n(%)	31(12.2)	127(12.6)	0.8
Current lipid lowering,n(%)	47(18.5)	171(16.9)	0.5
Any Other DMARD, n (%)	211(83)	772(76.6)	0.03

^{*} P-values were adjusted (P_{adj}) for age, sex, duration, ethnicity and if the patients were currently on lipid lowering medications, bmi, smoking or other DMARDS. P-value model examining plasma glucose additionally adjusted for diabetes medications.

⁺⁺ Erythrocyte sedimentation rate (ESR) was unavailable for 20 patients; of these 4 were currently taking HCQ and 16 were not.

^{**} Articular data was unavailable on 13 patients; of these 12 were not currently taking HCQ and 1 was not.

[§]DAS28ESR was unavailable for 29 patients. Of these 5 were currently taking HCQ and 24 were not.

[#]Sharp score was unavailable for 394 patients. Of these 73 were currently taking HCQ, and 321 were not.

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Table 2

Pooled follow-up visits of 1,261 RA patients divided by HCQ exposure

	None	Some Visits	All Visits	P _{adj} [*]
No of patients/No of visits	836/2911	316/1394	109/300	
Female, n(%)	2127 (73)	1,049 (75)	239 (80)	
Non-Hispanic White, n(%)	1,059 (36)	372 (26)	123 (40)	
Duration of RA, mean ± SD	15.3 ± 10.9	13.3 ± 9.3	11.9 ± 9.5	0.001, 0.001
Laboratory				
Total Cholesterol mg/dl, mean (SD)	185.7 ± 40.5	182.0 ± 38.0	181.0 ± 35.8	0.031, 0.01
LDL mg/dl, mean (SD)	106.5 ± 33.7	103.0 ± 30.7	97.22 ± 29.8	0.026, <0.001
HDL mg/dl, mean (SD)	52.8 ± 16.3	54.5 ± 17.2	60.6 ± 18.4	0.121, <0.001
Triglycerides mg/dl, mean (SD)	131.5 ± 80.6	123.1 ± 63.0	114.7 ± 56.9	<0.001, <0.001
Total Cholesterol/HDL, mean (SD)	3.80 ± 1.5	3.60 ± 1.3	3.21 ± 1.1	0.001, <0.001
LDL/HDL, mean (SD)	2.21 ± 1.1	2.09 ± 1.1	1.76 ± 0.8	0.04, <0.001
Plasma glucose mg/dl, mean (SD)	103.0 ± 38.7	101.9 ± 37.6	95.1 ± 30.4	0.77, 0.09
ESR mg/dl, mean (SD)	29.0±25.2	32.5±26.9	21.9±23.4	0.01, 0.04
Clinical				
Tender joints, mean (SD) ^{**}	7.45 ± 8.4	8.5 ± 8.7	6.36 ± 7.2	0.48, 0.31
Swollen joints, mean (SD) ^{**}	2.04 ± 3.7	2.51 ± 3.8	1.43 ± 2.8	0.39, 0.007
Deformed joints, mean(SD) ^{**}	8.42 ± 8.4	9.70 ± 8.7	5.69 ± 6.7	0.003, 0.066
DAS28ESR ^{\$}	3.99 ± 1.6	4.22 ± 1.6	3.48 ± 1.61	0.7, <0.001
Sharp Score [#]	82.5 ± 95.2	94.9 ± 101.3	46.1 ± 71.8	0.013, 0.009
Diabetes Med, n (%)	448 (15.4)	249(17.9)	47(15.7)	0.56, 0.67
Current Lipid Lowering, n(%)	755 (25.9)	288 (20.7)	67 (22.4)	0.15, 0.62
Any Other DMARD, n (%)	2141 (73.5)	1069 (76.7)	253 (84.3)	0.54, 0.07

^{*} P-values were obtained from GEE regression models for clinical comparison, models were adjusted for age, sex, RA duration, ethnicity, bmi, smoking, and lipid and DMARD medications. For laboratory comparisons p-value were adjusted for propensity scores.

^{**} We were unable to obtain articular data at all visits on 147 patients. of these 116 patients were never exposed to HCQ; 24 were intermittently exposed; and 7 were continuously taking HCQ.

^{\$} We were unable to obtain both articular data and ESR at all visits on 177: of these 134 patients were never exposed to HCQ; 33 were intermittently exposed; 10 were continuously taking HCQ.

[#] We were unable to obtain hand radiographs at all visit on 987: of these 670 were never exposed to HCQ; 273 were intermittently exposed; 44 were continuously taking HCQ.

Table 3

Association of HCQ with lipids in 5045 study visits

	Currently taking HCQ (n=929)	Not Currently Taking HCQ (n=4116)	P*
Laboratory			
Total Cholesterol mg/dl, mean (SD)	178.9 ± 38.0	185.6 ± 41.4	0.0001
LDL mg/dl, mean ± SD	98.0 ± 30.3	106.7 ± 33.2	<0.0001
HDL mg/dl, mean ± SD	58.9 ± 18.6	52.6 ± 16.4	<0.0001
Triglycerides mg/dl, mean ± SD	115.7 ± 62.2	135.7 ± 93.0	<0.0001
Total Cholesterol/HDL, mean ± SD	3.3 ± 1.3	3.8 ± 1.5	<0.0001
LDL/HDL, mean ± SD	1.8 ± 1.0	2.2 ± 1.1	<0.0001

* P-Value were obtained through GEE regression and was adjusted for age, sex, duration, ethnicity, and if the patients were currently on lipid lowering medications or other DMARDS.