Hospitalization with Hydroxychloroquine Initiation in Patients with Heart Failure with Preserved Ejection Fraction and Autoimmune Disease

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Introduction

Hydroxychloroquine (HCQ) is commonly used for the management of several autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus, and Sjogren syndrome. Previously, some observational studies have reported that HCQ is associated with increased risk of heart failure (HF).

Objective: To assess association of HCQ initiation with HF-related and all-cause hospitalizations among patients with heart failure and preserved ejection fraction (HFpEF).

Methods

- **Study Design**: Retrospective Cohort Study
- **Data Source:** IBM® MarketScan® claims databases
- **Study Period**: 01-01-2007 to 12-31-2019
- **Study Population:** Patients aged ≥18 years with diagnosed HFpEF and autoimmune disease. Patients were required to initiate HCQ after their first HFpEF diagnosis (HCQ users) or not (HCQ non-users).
- **Index Date:** The first HCQ prescription date was assigned as the index date. Index date for the HCQ non-user group was assigned by a prescription-time distribution matching HCQ users, utilizing the number of days from HFpEF diagnosis to the first HCQ prescription.
- **Study Outcomes:** HF-related and all-cause hospitalizations
- **Statistical Analysis:**
  After 1 up to 3 propensity score (PS) matching, Cox proportional hazards regression models were used to compare study outcomes between the HCQ users and non-users.

Results

- After PS matching, we identified 597 patients with hydroxychloroquine initiation after receiving a diagnosis of HFpEF and 1640 patients with no history of using hydroxychloroquine, for a final cohort of 2237 patients (Table 1).
- The study population had mean (SD) age of 67.2 (12.8) years, and 1,690 (75.5%) women.
- The most prevalent autoimmune diseases were rheumatoid arthritis (59.8%), systemic lupus erythematosus (10.4%), and Sjogren's Syndrome (5.0%).
- HCQ use was associated with 59% reduced risk of HF-related and 16% reduced risk of all-cause hospitalization as compared to non-use.

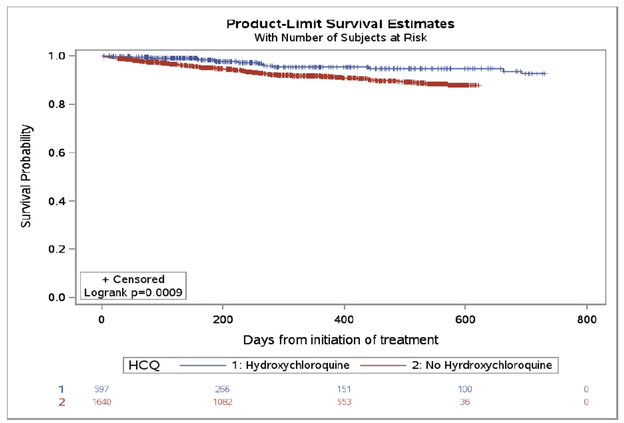
Table 1. Risk of HF-related and All-cause Hospitalization among Users vs Nonusers of Hydroxychloroquine in Patients with HFpEF and Autoimmune Disease

HCQ use	Patients, No.	Follow-up period, mean (SD), mo	Person-months	Events, No.	Crude incidence per 100 person-months	HR (95% CI)
HF-related Hospitalization						
Users	597	16.8 (7.9)	5,258	17	0.32	0.41 (0.24-0.71)
Nonusers	1,640	10.6 (6.2)	16,431	122	0.74	Reference
All-cause Hospitalization						
Users	597	16.8 (7.9)	3,938	221	4.90	0.84 (0.71-0.98)
Nonusers	1,640	10.6 (6.2)	12,204	707	5.79	Reference

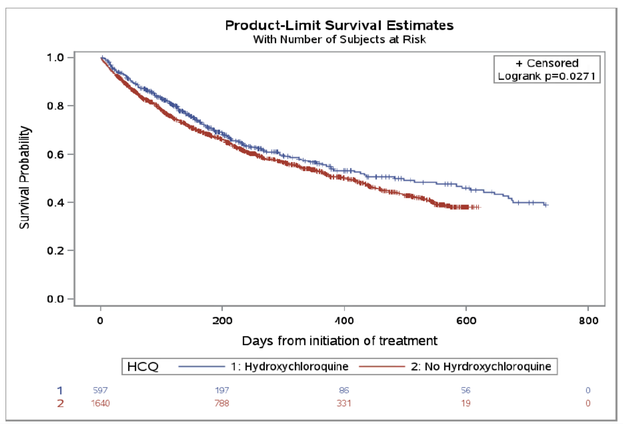
Abbreviation: CI, confidence interval; HCQ, hydroxychloroquine; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; SD, standard deviation.

Figure 1. Probability of HF-related and all-cause Hospitalization Among Users vs Nonusers of Hydroxychloroquine in Patients with HFpEF and Autoimmune Disease

HF-related Hospitalization



All-cause Hospitalization



Strengths

- First real-world study on assessing association of hydroxychloroquine with HF-related and all-cause hospitalizations among patients with HFpEF and autoimmune disease.
- Large commercial database representative of the US population covered under employer-based medical insurance.

Conclusions

Among patients with HFpEF and autoimmune disease, hydroxychloroquine use was associated with decreased risk of HF-related and all-cause hospitalizations.

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