The Impact of Untreated Hepatitis C Infection on Chronic Kidney Disease Progression

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Objective

- To determine whether untreated hepatitis C virus (HCV) infection accelerates renal decline and development of end-stage renal disease (ESRD) among patients with chronic kidney disease (CKD)

Methods

- ***Study population:*** Patients ≥18 years of age with incident untreated HCV and CKD diagnoses from 1/1/2004 to 12/31/2014 from KPSC and KPMAS
- ***Definition of CKD:*** Identified by 2 occasions of eGFR (estimated glomerular filtration rate, using the CKD-EPI definition) <60 mL/min/1.73 m^2 that are >90 days apart, with eGFR never returning ≥60
- ***Definition of HCV:*** Identified by at least one of: positive HCV RNA, detectable HCV genotype, or positive HCV antibody test plus ≥1 HCV-coded visit
- ***Definition of ESRD:*** Transplant approval, dialysis, or eGFR <15
- ***Definition of baseline:*** The year prior to index date (date of CKD or HCV diagnosis, the later of the two for the CKD + HCV cohort)
- ***Outcomes of interest:*** Rate of change in eGFR, time to a 25% decrease in eGFR, and time to ESRD
- ***Analytic approach:***
  - Generalized estimating equations (GEE), adjusting for covariates, compared the rate of change in eGFR between those with CKD + HCV vs CKD alone
  - Cox Proportional Hazards models, adjusting for covariates, compared the time to 25% decrease in eGFR and ESRD in those with CKD + HCV vs CKD alone
- ***Follow-up time:*** Censored at death, dialysis, kidney or liver transplant, or KP plan disenrollment. The ESRD model was censored on death and disenrollment

Funding: Study was funded by Merck & Co., Inc.
Conflicts of interest: JM Arduino is an employee and stockholder of Merck & Co., Inc.

Results

Table 1. Clinical and socio-demographic characteristics of patients with CKD + HCV compared to those with CKD alone

	CKD + HCV N=1,646	CKD Only N=150,625
Sex, n (%)		
Female	718 (43.6%)	81,660 (54.2%)
Male	928 (56.4%)	68,965 (45.8%)
Age at CKD index date		
Mean (SD)	65.7 (10.72)	71.4 (11.28)
Race, n (%)		
Asian/Native Hawaiian or Other Pacific Islander	78 (4.7%)	12,180 (8.1%)
Black or African	600 (36.5%)	22,133 (14.7%)
Hispanic	378 (23%)	26,198 (17.4%)
Multiple/Others	5 (0.3%)	486 (0.3%)
White	585 (35.5%)	89,628 (59.5%)
Comorbidities, n (%)		
History of type 1 and type 2 diabetes mellitus	680 (41.3%)	47,675 (31.7%)
Hypertension	1,167 (70.9%)	92,125 (61.2%)
HIV	60 (3.6%)	552 (0.4%)
Hepatitis B	26 (1.6%)	457 (0.3%)
Cirrhosis	437 (26.5%)	5,095 (3.4%)
Acute myocardial infarction	38 (2.3%)	3,781 (2.5%)
eGFR at baseline		
N	1,646	150,625
Mean (SD)	46.0 (11.41)	50.0 (8.09)
Median (Q1, Q3)	49 (41.0, 54.0)	52 (46.0, 56.0)
Number of follow-up eGFR measurements		
Mean (SD)	11.5 (10.84)	10.3 (10.07)
Total follow-up time (years)		
Mean (SD)	2.6 (2.31)	3.7 (2.85)

Patient Characteristics

- We identified 150,625 patients with CKD only and 1,646 patients with CKD + HCV. **Table 1** compares characteristics of patients with CKD+HCV to those with CKD alone

Impact of Untreated HCV Infection on CKD Progression

- eGFR declined by almost 1 more mL/min/1.73 m^2 per year, the hazard of a 25% decline in eGFR was approximately 1.5 times higher, and the hazard of ESRD was approximately 2.6 times higher in those with CKD + HCV compared to those with CKD alone

Table 2. Adjusted estimates comparing change in eGFR, hazard of 25% decline in eGFR, and hazard of ESRD in patients with CKD + HCV vs those with CKD alone

	Count With Outcome	Adjusted† Estimate (95% CI)
Change in eGFR (by year)	**—**	**-0.84 (-1.09, -0.60)**
Hazard of 25% decline in eGFR	**66,178**	**1.55 (1.43, 1.68)**
Hazard of ESRD	**5,628**	**2.59 (2.15, 3.11)**

†Models adjusted for age, sex, race/ethnicity, baseline eGFR, type I and II diabetes, hypertension, acute myocardial infarction, HIV, HBV, and CKD.

Discussion

- Untreated HCV infection has a substantial independent effect on renal decline among patients with CKD
- It remains to be seen whether the use of newer direct-acting HCV antivirals can mitigate the magnitude and rate of renal decline and progression to ESRD among patients with HCV and CKD

Limitations

- If there are additional comorbidities or other factors associated with HCV that also increase risk of renal decline that were not included in the adjusted model, we may overestimate HCV risk