

HCV Treatment Eligibility in ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans)

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Abstract

Background: Treatment eligibility rates for hepatitis C virus (HCV) infection are unknown.

Methods: We assembled a national cohort of HCV-infected veterans-in-care from 1998-2003, using the VA National Patient Care Database for demographic/clinical information, Pharmacy Benefits Management database for pharmacy records and the Decision Support Systems database for laboratory data. We compared the HCV monoinfected and HCV-HIV coinfecting subjects for treatment indications and eligibility using the current treatment guidelines.

Results: Of the 86,530 subjects, 27,452 subjects with HCV and 1,225 with HCV-HIV coinfection had complete clinical and laboratory data. Of those, 74% and 85% had indications for therapy (detectable HCV RNA plus > 2 elevated serum aminotransferase levels) and within this group, 56.1% of the HCV monoinfected and 28.4% of the HCV-HIV coinfecting subjects were eligible for treatment (had no contraindications to treatment). Anemia, decompensated liver disease (DLD), chronic obstructive pulmonary disease (COPD), recent alcohol abuse and coronary artery disease were the most common contraindications in the former and anemia, DLD, renal failure, recent drug abuse and COPD in the latter group. Among those eligible for treatment, only 23% of the HCV monoinfected and 15% of the HCV-HIV coinfecting subjects received any treatment for HCV.

Conclusions: Most veterans with HCV are not eligible for treatment according to the current guidelines. Even in those who are eligible for treatment, a minority is prescribed treatment. Several contraindications are modifiable and aggressive management of those may improve treatment prescription rates.

Introduction

- The current standard of care treatment for chronic HCV is pegylated interferon alfa plus ribavirin
- However, most HCV infected persons are not initiated on treatment,¹⁻⁷ and when initiated are unable to complete a full course⁸
- Treatment is indicated in patients with persistent HCV RNA viremia, and with some degree of liver damage
- Presence of certain medical and psychiatric comorbidities including chronic kidney disease, active or uncontrolled depression, severe anemia, autoimmune disease, active substance abuse, significant coronary artery disease and decompensated cirrhosis are considered contraindications to treatment.
- Determining the proportion of HCV infected subjects who are eligible for treatment according to the current guidelines is essential in planning effective intervention strategies at the population level.
- We determined the rate of treatment eligibility and contraindications to treatment in ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans), a national database of HCV infected veterans in care at any of the Veterans Health Administration (VA) healthcare facilities.

Methods

- We assembled a national cohort of HCV infected veterans from the VA National Patient Care Database (NPCD), the VA Pharmacy Benefits Management (PBM) data and the Decisions Support System Database (DSS) between VA fiscal years (FY) 1998-2003 (October 1, 1997 through September 30, 2003). (Figure 1)
- Our primary outcome measure was eligibility for treatment for HCV in the HCV monoinfected and HCV-HIV coinfecting subjects based on the definitions provided below.
- The criteria for eligibility (presence of indications AND absence of contraindications for treatment) were adapted from current treatment guidelines for HCV.⁹⁻¹¹ (Table 1)
- Subjects were considered to have HCV infection if at least one antibody test, or a qualitative or quantitative HCV RNA by PCR was positive.
- We determined a subject to have an indication present for treatment if the HCV RNA was detectable by the standard assay being used by the local laboratory AND the serum alanine or aspartate aminotransferase (ALT or AST) level above 40 IU/ml on ≥ 2 occasions prior to any initiation of treatment for HCV.
- We then determined the presence of contraindications to treatment. The list of comorbid conditions considered a contraindication to treatment is provided in table 1, along with the operational definitions used in this study.
- Prescription for HCV was defined as having received a prescription for interferon alfa, pegylated interferon alfa or a combination of either plus ribavirin for any duration of time.
- To test for any bias in our final evaluable sample, we compared the demographics of our final sample with the subjects who were excluded based on non-availability of complete laboratory data. We also determined the prevalence of contraindications in the group of subjects with HCV infection diagnosed based on at least one inpatient and two outpatient codes, and who had evidence of liver injury based on elevation of serum ALT/AST levels.
- We compared the presence of indications and contraindications for treatment in the HCV monoinfected and HCV-HIV coinfecting subjects. The demographic characteristics were compared using the chi-square or the t-test as appropriate. Proportion of subjects with each contraindication was compared between the two groups using the chi-square test. We used Stata © (version 9.2, College Station, TX) for all statistical analyses.

Results

Table 1. Operational definitions of contraindications to HCV therapy used for the current study. (list of contraindications adapted from references⁹⁻¹¹)

Contraindications to HCV treatment	Operational definition
Life threatening medical illness: <ul style="list-style-type: none"> Malignancy Coronary artery disease Chronic obstructive pulmonary disease Uncontrolled seizures Autoimmune disorders 	≥ 2 ICD-9 codes any time prior to treatment ≥ 2 ICD-9 codes within last 12 months ≥ 2 ICD-9 codes within last 12 months ≥ 2 ICD-9 codes within last 12 months ≥ 2 ICD-9 codes for rheumatoid arthritis, systemic lupus erythematosus, autoimmune hepatitis, any time prior to treatment
Decompensated liver disease	Any of the following at anytime prior to treatment or last observation date, whichever came first: <ul style="list-style-type: none"> INR >1.3 Albumin <2.5 g/dl Diagnosis of esophageal varices, ascites, hepatic encephalopathy Total bilirubin > 2.0 mg/dl
Active psychiatric illness	any 1 inpatient admission with condition listed as primary reason for admission, OR 2 or more clinic visits to a psychiatric clinic within 12 months prior to entering the cohort, or any time during follow up
Recent alcohol abuse	Any primary alcohol related admission (e.g. alcohol withdrawal syndrome, delirium tremens, alcohol rehab admission, etc. with condition listed as primary reason for admission) within 12 months prior to entering the cohort, or any time during follow-up
Recent drug use	any 1 inpatient admission with condition listed as primary reason for admission, OR 2 or more clinic visits to a drug rehabilitation clinic within 12 months prior to entering the cohort, or any time during follow up
Renal failure	Serum creatinine > 1.5 mg/dl collected as an outpatient
Uncontrolled diabetes	≥ 2 glucose levels > 250 mg/dl within 12 month prior to entering cohort or any time during follow up (only outpatient values)
Moderate to severe anemia	Hemoglobin < 12 g/dl for men, <11.0 g/dl for women, within 12 months prior p to treatment date or last observation date
Neutropenia	Total WBC count < 1.5 x 10 ³ cells/mm ³
Heart, lung, kidney transplant	ICD-9 code or related diagnostic code(timeframe?) at ANY TIME prior to HCV treatment; if no HCV treatment, then at ANY TIME
Advanced HIV disease	Lowest CD4 count <100 per mm ³

Table 2. Characteristics of HCV and HCV/HIV coinfecting subjects with and without HCV RNA availability.

DEMOGRAPHICS	HCV+ (n=27,452)	HCV+/HIV+ (n=1,225)	
Mean (SD) age, years	50.5 (7.8)	48.6 (6.0)	<0.001
Race			<0.001
White	46.4	23.8	
Black	23.9	53.3	
Hispanic	6.3	12.4	
Other/unknown	23.4	10.5	
Gender (%male)	96.8	98.4	<0.001
Liver biopsy performed	1.9	1.8	0.4
Referred to GI	65.4	43.4	<0.001
CONTRAINDICATIONS			
Anemia (Hb<12 for men, <11 for women)	17.5	42.7	<0.001
Autoimmune disorders	1.6	0.3	<0.001
Chronic obstructive pulmonary disease	14.8	12.5	0.2
Coronary artery disease	12.0	7.9	<0.001
Decompensated liver disease	14.4	26.4	<0.001
Neutropenia	0.4	3.3	<0.001
Organ transplant	1.7	3.8	<0.001
Active psychiatric disease	6.5	9.5	<0.001
Recent alcohol use	11.9	10.2	0.008
Recent drug use	6.3	13.4	<0.001
Renal failure (serum Cr >1.5)	8.8	19.1	<0.001
Seizures	4.9	5.6	0.003
Uncontrolled diabetes	8.0	7.8	0.1
At least one contraindication present	54.8	70.1	<0.001

Figure 1. Data sources and creation of ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans).

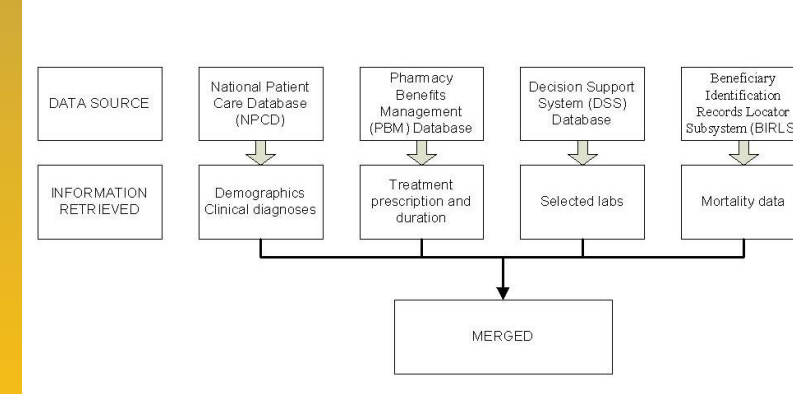


Figure 2. Flowchart of treatment eligibility and contraindications in the HCV monoinfected subjects.

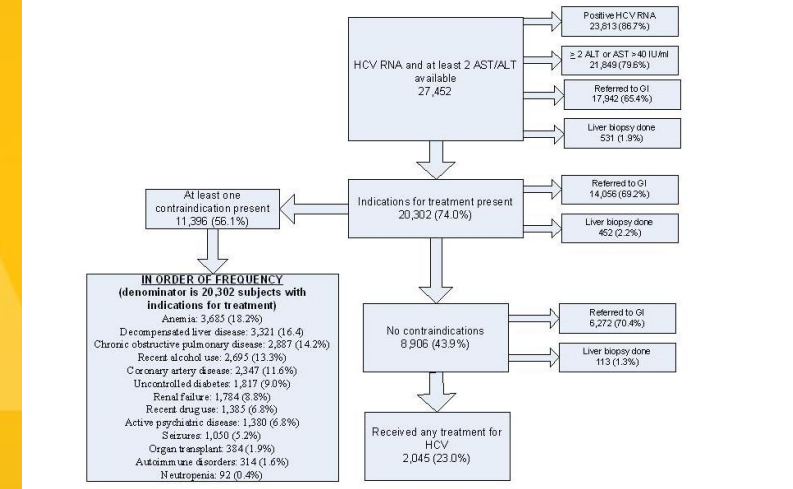


Figure 3. Flowchart of treatment eligibility and contraindications in the HCV-HIV coinfecting subjects.

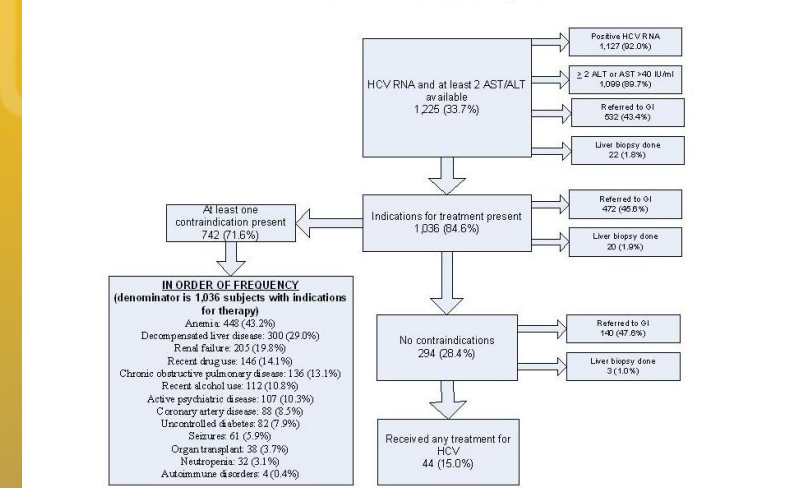
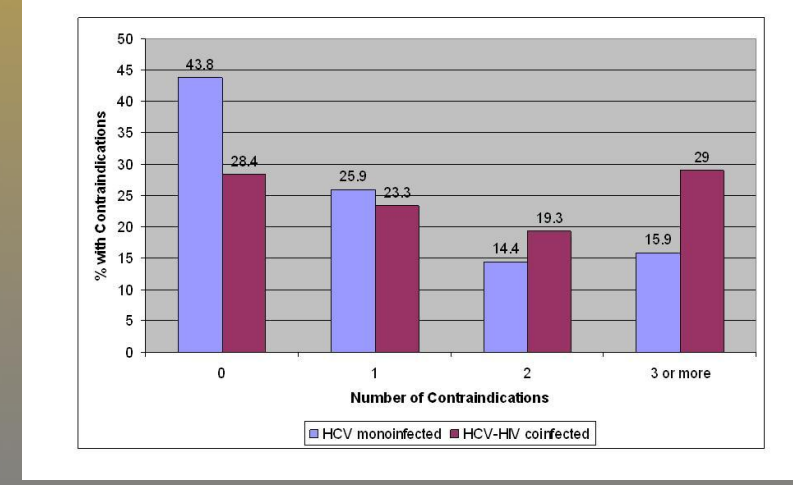


Figure 4. Number of contraindications by group.



Conclusion

- Even when indications for pharmacotherapy were present, a majority of subjects in both HCV monoinfected and HCV-HIV coinfecting groups were ineligible for treatment due to presence of at least one contraindication.
- HCV-HIV coinfecting persons were less likely to be eligible for treatment compared with the HCV monoinfected subjects.
- Our finding that only ~44% of the HCV monoinfected and ~28% of the HCV-HIV coinfecting persons were eligible for treatment should prompt healthcare providers and policy makers to address the modifiable contraindications to optimize care of this population.
- Even among those eligible for therapy, only a small number was prescribed treatment in either group.

Reference List

- Butt AA, Justice AC, Skanderson M, Good CB, Kwoh CK. Rates and Predictors of HCV Treatment in HCV-HIV Coinfected Persons. *Alimentary Pharmacology and Therapeutics* 2006; 24:585-591.
- Butt AA, Wagener M, Shakil AO, Ahmad J. Reasons for Non-treatment of Hepatitis C in Veterans in Care. *Journal of Viral Hepatitis* 2005; 12:81-85.
- Butt AA, Justice AC, Skanderson M, Rigsby M, Good CB, Kwoh CK. Rate and Predictors of Treatment Prescription for Hepatitis C. *Gut* 2007; 56(3):385-389.
- Hallinan R, Byrne A, Agho K, Dore GJ. Referral for chronic hepatitis C treatment from a drug dependency treatment setting. *Drug Alcohol Depend* 2007; 88(1):49-53.
- Irving WL, Smith S, Cater R et al. Clinical pathways for patients with newly diagnosed hepatitis C - what actually happens. *J Viral Hepat* 2006; 13(4):264-271.
- Zinkernagel AS, von W, V, Ledergerber B et al. Eligibility for and outcome of hepatitis C treatment of HIV-coinfected individuals in clinical practice: the Swiss HIV cohort study. *Antivir Ther* 2006; 11(2):131-142.
- Morrill JA, Shrestha M, Grant RW. Barriers to the treatment of hepatitis C. Patient, provider, and system factors. *J Gen Intern Med* 2005; 20(8):754-758.
- Butt AA, Skanderson M, McGinnis KA, Kwoh CK, Justice AC. Real-life Rates of Treatment Completion for HCV. 58th Annual Meeting of the American Association for the Study of Liver Diseases, November 2-6, 2007 Boston, MA. 2007.
- Yee HS, Currie SL, Darling JM, Wright TL. Management and treatment of hepatitis C viral infection: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center program and the National Hepatitis C Program office. *Am J Gastroenterol* 2006; 101(10):2360-2378.
- NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consensus State Sci Statements* 2002; 19(3):1-46.
- APASL Hepatitis C Working Party. Asian Pacific Association for the Study of the Liver consensus statements on the diagnosis, management and treatment of hepatitis C virus infection. *J Gastroenterol Hepatol* 2007; 22(5):615-633.