Published in final edited form as:
J Clin Gastroenterol. 2013 ; 47(5): 457–460. doi:10.1097/MCG.0b013e318266fe70.

Willingness to Undergo a Repeat Liver Biopsy among HIV/Hepatitis C Virus-Coinfected and Hepatitis C Virus-Monoinfected Patients

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Abstract

Background—Guidelines for chronic hepatitis C virus (HCV) management have recommended that a liver biopsy be repeated at 3-year intervals for HIV/HCV-coinfected patients and 5-year intervals for those with HCV monoinfection to assess fibrosis progression. However, it is unclear if patients are willing to repeat this procedure.

Objective—To determine the prevalence and factors, particularly HIV coinfection, associated with willingness to repeat a liver biopsy.

Methods—A questionnaire was administered to 235 HCV-infected patients (113 with HIV coinfection) between January 2008 and June 2011who previously underwent liver biopsy. The main outcome was self-reported willingness to repeat the biopsy. The questionnaire collected data on other hypothesized determinants of willingness to repeat the biopsy. These were evaluated by logistic regression.

Results—Among 235 subjects who completed the questionnaire, 32 (14%) reported unwillingness to repeat the biopsy, most commonly due to a perception that it was unimportant for care (13[41%]), concerns regarding pain (12[38%]), and a poor experience with the prior biopsy (7[21%]). Considering biopsy to be safe (OR, 4.45; 95% CI, 1.50–13.27), important (OR, 4.87; 95% CI, 1.83–12.95), and knowing a person who underwent liver biopsy (OR, 3.45; 95% CI,

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Potential conflicts of interest: None to report.

The results were presented in part at the 16th Conference on Retroviruses and Opportunistic Infections, February 8–11, 2009, Montreal, Canada [Abstract 846].

1.16–10.23) were associated with willingness to repeat the biopsy. HIV was not associated with willingness to repeat the biopsy (OR, 1.42; 95% CI, 0.67–3.03).

Conclusions—14% of chronic HCV-infected patients were unwilling to repeat a liver biopsy. HIV was not associated with unwillingness. In patients in whom a repeat liver biopsy is indicated, education on the utility and safety of the biopsy is important to its acceptance.

INTRODUCTION

Historically, a percutaneous liver biopsy has been the traditional method used to evaluate hepatic damage associated with chronic hepatitis C virus (HCV) infection. The liver biopsy can: 1) determine the stage of fibrosis and grade of hepatic inflammation, 2) identify concurrent disease processes (e.g., steatosis, iron overload) that can contribute to hepatic injury, and 3) aid in the decision to initiate HCV treatment.[1] Because liver fibrosis progression is variable and may be influenced by such co-factors as age, alcohol intake, use of hepatotoxic medications, and HIV coinfection, a longitudinal assessment of HCV-associated liver fibrosis can help guide initiation of HCV therapy among untreated patients and those who did not achieve virologic cure to a previous treatment regimen.[2–4] As a result, guidelines have suggested that a liver biopsy be repeated at 3-year intervals for HIV/HCV-coinfected patients and 4- to 5-year intervals for HCV-monoinfected patients to evaluate fibrosis progression.[5,6] While direct and indirect biochemical markers of liver injury and imaging techniques are improving in their ability to appropriately stage hepatitis C-related liver disease and liver biopsy is subject to limitations, the test remains the current albeit imperfect gold standard for staging liver disease.[7,8]

Absent from all current guidelines, however, are data examining chronic HCV-infected patients' willingness to undergo repeated liver biopsies. In particular, the prevalence and factors associated with willingness to repeat this procedure are unknown. In particular, it remains unclear if HIV coinfection increases reluctance to repeat the liver biopsy. HIV coinfection might add physical and psychological stress that reduces willingness to undergo a repeat liver biopsy. To address this issue, we compared HIV/HCV-coinfected and HCV-monoinfected patients' willingness to undergo a repeat liver biopsy and evaluated additional determinants of willingness to repeat the procedure.

PATIENTS AND METHODS

Study Design and Subjects

We performed a cross-sectional study among chronic HCV-infected patients referred for evaluation at the viral hepatitis clinics of Penn Presbyterian Medical Center and Philadelphia Veterans Affairs (VA) Medical Center in Philadelphia, PA. HCV-infected patients were eligible if they had: 1) detectable HCV RNA, 2) documented HIV status by HIV antibody or RNA test, 3) prior liver biopsy, and 4) at least one hepatitis clinic visit documented in their medical record. Eligible subjects were identified by reviewing: 1) lists of patients who underwent a liver biopsy at both sites, and 2) results of laboratory tests for HCV RNA and HIV infection generated from computerized laboratory records. Eligible patients were invited to participate in the study as they presented to the clinics. The study was approved by

the Institutional Review Boards of the University of Pennsylvania and Philadelphia VA Medical Center.

Main Outcome Measures

The main study outcome was self-reported willingness to undergo a repeat liver biopsy. Each subject was asked, “If your health care provider recommended that you repeat the liver biopsy to evaluate your chronic hepatitis C, would you be willing to repeat the biopsy?” The respondent had the option of answering “Yes,” “No,” or “Don’t Know.”

Data Collection

Data were collected from medical records and an interviewer-administered questionnaire. Data abstracted from charts included: age at study visit, sex, concomitant medical and psychiatric diagnoses, HCV-related information (i.e., year of HCV diagnosis, HCV transmission risk factors, HCV genotype, HCV RNA level, date of prior liver biopsy, fibrosis stage and inflammation grade from prior liver biopsy), HIV status, and HIV infection data (i.e., year of HIV diagnosis, antiretroviral therapy use, HIV RNA level, and CD4 T lymphocyte count).

Perceptions about the liver biopsy were obtained from an interviewer-administered questionnaire. A total of 20 patients (10 from each site; 5 coinfected and 5 monoinfected) participated in an open focus group to help frame the study items and responses. A facilitator asked patients about their understanding of the liver biopsy, their concerns prior to undergoing the procedure, and about their overall experience. Nominal group techniques, particularly open-ended questions, were employed to ensure that items and responses were generated, described, and prioritized by patients with chronic HCV who underwent a liver biopsy. A list of possible factors associated with unwillingness to repeat the liver biopsy was generated. The questionnaire was then administered in pilot testing to a separate set of 10 patients (5 from each site; 5 coinfected and 5 monoinfected), who were then asked by the facilitator to explain their results. These discussions allowed the questions and responses to be revised further. The final questionnaire included questions evaluating possible factors associated with willingness to repeat a liver biopsy, including race, ethnicity, level of education, current employment status, extent of knowledge about the liver biopsy, prior HCV treatment, and concerns about complications of the biopsy (see Appendix for questionnaire).

Statistical analysis

Differences in characteristics by HIV status were assessed using Chi-square or Fisher’s exact tests for categorical data and Wilcoxon rank-sum tests for continuous data. Logistic regression analysis examined associations (odds ratios [ORs] and 95% confidence intervals [CIs]) between hypothesized factors and willingness to undergo a repeat biopsy. All data were analyzed using SPSS 19.0 (IBM, Chicago, Ill).

RESULTS

Patient characteristics

Review of the lists of patients who previously underwent a liver biopsy at the two sites identified 239 patients who met eligibility criteria and were recruited for the study. Among these patients, 4 (2%) refused to participate, leaving 235 (113 HIV/HCV-coinfected) in the final sample.

The characteristics of these subjects are listed in Table 1. HIV/HCV-coinfected subjects were younger; more likely to have had a prior ultrasound-guided or transjugular liver biopsy; had fewer days since last biopsy; and less commonly received HCV therapy compared to HCV-monoinfected patients.

Liver biopsy perceptions

Thirty-two (14%) subjects reported that they were unwilling to repeat the liver biopsy and 203 (86%) reported that they were willing to repeat the biopsy. The most common reasons included perceptions that it was unimportant for care [13 (6%)], concerns regarding pain [12 (5%)], and having a poor prior experience [7 (3%)].

An analysis of the factors associated with willingness to undergo a repeat liver biopsy is shown in Table 2. Patients who considered the liver biopsy safe (OR, 4.45; 95% CI, 1.50–13.27), important (OR, 4.87, 95% CI, 1.83–12.95), and who knew someone who had a liver biopsy (OR, 3.45; 95% CI, 1.16–10.23) were more likely to be willing to repeat the biopsy. No difference in willingness to repeat the biopsy was observed between HIV/HCV-coinfected and HCV-monoinfected persons (100 [88%] versus 103 [84%]; OR for willingness to repeat, 1.42; 95% CI, 0.67–3.03). Other factors such as age, sex, race, psychiatric illness, education level, employment status, type of liver biopsy, time since liver biopsy, prior stage hepatic inflammation, or receipt of HCV therapy were not associated with willingness to repeat the biopsy.

DISCUSSION

In this study among chronic HCV patients who previously underwent a liver biopsy, we found that the majority of patients (86%) were willing to repeat the biopsy. Considering the biopsy safe and important to care, and knowing someone who had a liver biopsy were associated with willingness to repeat the procedure. Most commonly cited reasons for reluctance to repeat biopsy were the perception that it was not important for care and concerns for pain. HIV coinfection was not associated with unwillingness to repeat the liver biopsy. Although women were underrepresented in our study sample, there was a trend towards a lack of willingness to repeat the liver biopsy among women, and further study is needed to explore this potential gender difference. The high acceptance rate of liver biopsy in this study may be reflective of this study population in which liver biopsy was being recommended by practitioners with specialization in viral hepatitis who might have been able clearly explain the relevance of the procedure and subsequent biopsy results to HCV-infected patients.

The reluctance to repeat the liver biopsy because of the perception that it was unimportant for HCV care and the increased likelihood of agreeing to liver biopsy if one considers it safe or important suggests that interventions to improve knowledge about the procedure might increase liver biopsy rates for those in whom liver biopsy will influence management. Such educational interventions might include dedicated teaching sessions about the importance of biopsy to HCV care, handouts describing the biopsy, and pictures of the procedure aiming to explain how the biopsy is performed and its potential complications.

Our study had several limitations. First, this study could not control for the extent and quality of information conveyed to individual patients regarding the importance of biopsies. Second, our study was limited by the small number of subjects who reported unwillingness to undergo a repeat liver biopsy, which limited our ability to perform multivariable logisitic regression analyses. Additionally, subjects came from study sites in an urban setting and were predominantly male and African American, potentially limiting the generalizability of our results.

In an era in which new treatments for HCV promise to be safer and easier, improve rates of sustained virologic response, and decrease durations of therapy, the relevance of undergoing or repeating a liver biopsy is likely to diminish for the majority of patients. However, currently among the subset of patients with minimal or no fibrosis who may not receive clinical benefit from a still costly and difficult to tolerate course of hepatitis C therapy, close monitoring with serial biopsies over time may be of importance in order to accurately determine progression of fibrosis warranting initiation of hepatitis C therapy. In this context, ascertaining patient-specific barriers to repeat liver biopsy will be vital.

In conclusion, 14% percent of chronic HCV-infected patients were unwilling to repeat a liver biopsy. HIV-confection did not affect willingness to repeat the procedure, but considering the liver biopsy important and safe and having a friend who had a biopsy increased willingness to repeat the procedure. As a new era in HCV therapy arrives, additional research will be of importance in addressing the role and relevance of liver biopsy as a longitudinal assessment of hepatic fibrosis in HCV infected persons.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial support: National Institutes of Health research grant K01 AI070001 [to V.L.R.].

Abbreviations

HCV	hepatitis C virus
HIV	human immunodeficiency virus infection

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Table 1

Demographic and clinical characteristics of the study subjects.

Characteristic	All Subjects (N=235)	HCV-Monoinfected (n=122)	HCV/HIV-Coinfected (n=113)	P-value
Median age (yr ± sd)	54	56	52	< 0.001
Male sex (%, no.)	81% (191)	99(81%)	92(81%)	>0.5
Race (%, no.)				
Black	71% (167)	66% (80)	77%(87)	0.3
White	26% (62)	32% (39)	20% (23)	
IDU history	64% (151)	60% (73)	69% (78)	0.2
Education level (%, no.)				0.4
Less than high school	26% (61)	21% (26)	31% (35)	
High school graduate	37% (88)	39% (48)	35% (40)	
Some college	25% (58)	29% (35)	20% (23)	
Graduated college	4% (9)	3% (4)	4% (5)	
Graduate school	8% (19)	7% (9)	9% (10)	
Psychiatric disorder (%, no.)	54% (126)	55% (67)	53% (59)	0.7
Depression	43% (100)	42% (51)	43% (49)	0.7
Prior liver biopsy type (%, no.)				<0.001
Ultrasound-guided	63% (149)	52% (63)	76% (86)	
Blind percutaneous	23% (55)	38% (46)	8% (9)	
Transjugular	8% (18)	4% (5)	12% (13)	
Unknown	6% (13)	7% (8)	4% (5)	
Hepatic fibrosis (%, n.)				0.08
No or mild fibrosis	44% (103)	37% (45)	51% (58)	
Bridging fibrosis/cirrhosis	34% (79)	30% (49)	27% (30)	
Median days since prior liver biopsy (IQR)	775 (262–1813)	951 (327–2076)	555 (204–1413)	0.03
Median HCV RNA (IU/mL)	1,240,000	1,340,000	1,470,000	>0.5
Received HCV therapy	52% (123)	60% (73)	50 (44%)	0.02
Median CD4 count (cells/mm^3)	N/A	N/A	450 (IQR 269 – 565)	N/A
Antiretroviral use (%, no.)	N/A	N/A	94% (73)	N/A

HIV=human imunodeficiency virus; HCV=hepatitis C virus; IQR=interquartile range; N/A=not applicable

Table 2

Univariable analysis of factors associated with willingness to repeat the liver biopsy.

Determinant	Odds Ratio (95% CI)
Age (≤45 yrs vs. > 45 yrs)	2.20 (0.50 – 9.80)
Female sex	0.44 (0.19 – 1.02)
African-American race	0.96 (0.42 – 2.19)
HIV-coinfected	1.42 (0.67 – 3.03)
Prior history of injection drug use	1.48 (0.69 – 3.15)
History of psychiatric disease	1.11 (0.52 – 2.36)
At least high school graduate	1.99 (0.90 – 4.38)
Employed	0.75 (0.32 – 1.73)
Blind percutaneous vs. other method	0.75 (0.32 – 1.73)
Time since prior biopsy (<=1 year vs. >1 year)	1.13 (0.51 – 2.53)
Minimal fibrosis (METAVIR ≤F1or Ishak ≤F2)	1.03 (0.49 – 2.19)
Previously treated for chronic HCV infection	1.12 (0.53 – 2.35)
Interview questions:	
Considers the biopsy safe	4.45 (1.50 – 13.27)
Considers the biopsy important	4.87 (1.83 – 12.95)
Knows a friend who has had a biopsy	3.45 (1.16 – 10.23)

HIV=human immunodeficiency virus; HCV=hepatitis C virus infection