Risk of Echocardiographic Pulmonary Hypertension in Individuals with Human Immunodeficiency Virus–Hepatitis C Virus Coinfection

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Abstract

Rationale: Human immunodeficiency virus (HIV) infection is a risk factor for pulmonary hypertension (PH). Chronic hepatitis C virus (HCV) infection may have unique or synergistic effects on the pulmonary vasculature, but the prevalence and risk factors for PH in HIV-HCV coinfecting persons are not known.

Objectives: To define the prevalence of echocardiographic PH in a cohort of patients with HIV-HCV coinfection, to compare this estimate with the reported prevalence of PH among those with HIV infection alone, and to identify potential risk factors for PH in coinfecting individuals.

Methods: We performed a retrospective study of HIV-HCV coinfecting patients followed at our institution from 2003 to 2012 with evidence of HCV infection (positive HCV antibody, measurable HCV ribonucleic acid viral load, and/or genotype) within 6 months of transthoracic echocardiogram. PH was defined by an estimated pulmonary artery systolic pressure (PASP) of greater than or equal to 40 mm Hg or more than moderate right ventricular dysfunction. We excluded those diagnosed with cirrhosis, left ventricular ejection fraction less than 50%, or more than moderate aortic or mitral valve disease.

Measurements and Main Results: Sixty-eight patients were included, and 43 had adequate estimates of PASP. The median (interquartile range) age was 52 (48–57) years, and 45 (67%) were men. Eight (19%) had PH, and three (7%) had more than moderate right ventricular dysfunction. After age and sex adjustment, interferon (IFN)-based HCV treatment was associated with higher PASP (β , 6.00 mm Hg; 95% confidence interval, 0.09–11.90; $P = 0.047$) and with the risk of PH (odds ratio, 5.65; 95% confidence interval, 1.07–29.93; $P = 0.042$). These associations persisted after adjustment for comorbidities but were attenuated by adjustment for duration of HCV diagnosis.

Conclusions: The prevalence of echocardiographic PH may be higher in HIV-HCV coinfecting individuals than in those with HIV monoinfection. IFN-based HCV treatment and time since HCV diagnosis were associated with the development of PH as assessed by echocardiography. Further studies are needed to examine HIV-HCV coinfection, HCV treatment, and duration of infection as possible causes of pulmonary vascular disease.

Keywords: hepatitis C; human immunodeficiency virus; pulmonary hypertension; echocardiography; interferon

(Received in original form May 31, 2014; accepted in final form October 8, 2014)

Supported in part by the National Institute of Allergy and Infectious Diseases grant P30AI042853 (R.B.S., L.E.T., and F.G.), the American Heart Association grant 11FTF7400032 (C.E.V.), the National Heart, Lung, and Blood Institute grant T35 HL094308–03 (R.B.S.), and the National Institute of General Medical Sciences grant P20GM103652 (C.E.V.).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the American Heart Association or the National Institutes of Health.

Author Contributions: R.B.S.: contributed to study design, data procurement and analysis, and drafting and revisions of the manuscript. C.E.V.: contributed to study concept and design, data analysis, and drafting and revisions of the manuscript. L.E.T.: contributed to study design, data procurement, and review of the manuscript. F.G.: contributed to data procurement and review of the manuscript. A.P.: contributed to data procurement and review of the manuscript. J.R.K.: contributed to study concept and design and review of the manuscript.

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This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org

Ann Am Thorac Soc Vol 11, No 10, pp 1553–1559, Dec 2014

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DOI: 10.1513/AnnalsATS.201405-225OC

Internet address: www.atsjournals.org

Pulmonary hypertension (PH) is a disease state of the pulmonary vasculature resulting in increased pulmonary vascular resistance, ultimately leading to right ventricular (RV)

failure and death. A variety of systemic illnesses have been associated with PH, including human immunodeficiency virus (HIV) infection (1, 2). Over the past two decades,

multiple studies have estimated the prevalence of PH in patients with HIV to be approximately 0.5% (3–5). Although rare, PH complicating HIV infection has not decreased appreciably

with available antiretroviral therapy (ART), and the mechanistic link between PH and HIV has not been clearly established (4). Although HIV ribonucleic acid (RNA) has not been isolated in the pulmonary vasculature, HIV proteins such as Tat and Nef cause endothelial dysfunction (6–12). It stands to reason that other viral infections may cause downstream fibroproliferation and remodeling in the pulmonary circulation.

It is estimated that 30% of patients in the United States infected with HIV are coinfecting with chronic hepatitis C virus (HCV) (13). Although it is speculated that HCV may be a risk factor for the development of PH (independent of HIV and/or portopulmonary hypertension), this has not been well studied (6). It is possible that chronic HCV infection is an independent risk factor for PH but also that the risk of PH with HIV-HCV coinfection is additive. Intravenous morphine exposure and simian immunodeficiency virus (SIV) act synergistically to promote pulmonary vasculopathy in macaques (14). Injection drug use (IDU) is the most common mode of HCV transmission in the United States, and HIV-HCV coinfection rates among patients with IDU are greater than 50% (15, 16). More recently, it has been suggested that interferon (IFN), historically the mainstay of therapy for chronic HCV infection, may be a unique risk factor for drug-induced pulmonary arterial hypertension (2, 17–19).

The aim of this study was to define the prevalence of echocardiographic PH in a cohort of patients with HIV-HCV coinfection and to identify potential risk factors for PH in coinfecting individuals. We hypothesized that the prevalence of PH or RV dysfunction by echocardiogram would be higher in individuals with HIV-HCV coinfection than the reported prevalence of PH in HIV-infected persons alone and that IFN-based treatment for HCV would be a significant risk factor for PH (1–5).

Methods

Study Design

We conducted a retrospective study of HIV-HCV coinfecting patients followed in the Miriam Hospital Immunology Center Database (ICDB) in Providence, Rhode Island from 2003 to 2012. The Miriam

Hospital Immunology Center is a Ryan White Program–funded HIV clinic with 1,500 HIV-infected adults in total. We included individuals with documented HCV infection (defined by a positive HCV antibody, a measurable HCV RNA viral load, and/or genotype) within 6 months of trans-thoracic echocardiogram (20). Patients were excluded if they had a physician-reported history of cirrhosis and/or evidence of significant left heart dysfunction, as noted below. The study was approved by the Rhode Island Hospital Institutional Review Board and The Miriam Hospital Immunology Center (IRB #205712).

Echocardiograms

Coinfecting patients were included if they had available transthoracic echocardiograms and if these echocardiograms were performed after HCV treatment was initiated. All echocardiograms were performed at the Echocardiography and Stress Testing laboratory in the Cardiovascular Institute of Lifespan. Right atrial pressure was derived based on size and response to respiratory changes, and pulmonary artery systolic pressure (PASP) was then estimated by adding right atrial pressure to the peak tricuspid regurgitant jet velocity converted to pressure according to the modified Bernoulli equation, as per American Society of Echocardiography guidelines (21). Estimated PASP was recorded as a continuous measure. RV function was graded as normal, mild, moderate, or severe by echocardiography readers and recorded as such. PH was defined by a PASP greater than or equal to 40 mm Hg or more than moderate RV dysfunction. Left atrial enlargement was defined as greater than or equal to 3.8 cm for women and greater than or equal to 4.0 cm for men (22). Diastolic dysfunction and estimated left atrial pressure were assessed by integrating mitral valve Doppler inflow velocity measurements with pulmonary vein Doppler pattern and mitral annular tissue Doppler diastolic measurements (23). Diastolic dysfunction was designated when more than grade II diastolic dysfunction (mitral E/A ratio ≥ 1 and average E/e' ratio > 10) was present. We excluded those with left ventricular ejection fraction less than 50% and/or more than moderate mitral or aortic valve disease.

Variables of Interest

Data were extracted from the ICDB and by chart review. Baseline characteristics, including age, sex, race/ethnicity, and date of HIV and HCV diagnoses, were collected from the ICDB. HIV parameters were obtained via chart review, including CD4⁺ cell count, HIV viral load, and ART status. Similarly, HCV parameters, such as HCV viral load, treatment status and regimen (i.e., IFN, ribavirin, additional oral agents), sustained virologic response (SVR) (negative HCV viral load at least 6 months after the cessation of treatment), and genotype, were collected (20). Comorbid illnesses (i.e., systemic hypertension, diabetes mellitus, airways disease [asthma, chronic obstructive pulmonary disease, and/or emphysema]) as recorded in the medical record and laboratory values (i.e., hemoglobin, creatinine) that could impact the risk of PH or right heart dysfunction were also collected. Whenever possible, covariates were assessed at the time or within 6 months of echocardiogram.

Statistical Analysis

Continuous variables were expressed as median (interquartile range [IQR]), and categorical variables were expressed as percentages. Independent sample *t* tests were used to compare continuous variables and chi-square or Fisher exact tests were used to compare categorical variables, as appropriate. Bivariate and multivariate linear and logistic regression were used to assess the relationship between clinical factors, including comorbid illnesses and HIV-HCV covariates, and PASP and the presence of PH or RV dysfunction, respectively. To avoid overfitting, final models included adjustment for age and sex. Potential confounding variables were added sequentially to this base model if $P < 0.20$ in bivariate analyses. Data were collected using Excel 2007 (Microsoft, Redmond, WA), and analyses were performed using STATA 10.0 (StataCorp, College Station, TX). Statistical significance was defined as $P < 0.05$.

Results

A total of 357 HIV-HCV coinfecting patients were followed at the Miriam Hospital Immunology Center from 2003 to 2012. Of

these, 93 (26%) had echocardiograms available (Figure 1). Six (6%) and 15 (16%) patients were excluded from analysis due to liver cirrhosis and significant left-sided or valvular dysfunction, respectively. Four (4%) received HCV treatment after echocardiogram and were also excluded. Of the remaining 68 coinfecting patients, 43 (63%) had echocardiograms. Of these 43, 8 (19%) had echocardiographic PH and 3 (7%) had more than moderate RV dysfunction (but did not have PASP estimated).

Characteristics of the study sample and those with and without PH are shown in Table 1. The median (IQR) age was 52 years (48–57 yr), 45 (67%) were men, and 36 (53%) were white. The majority were current smokers (53 [78%]) and had a history of IDU (39 [57%]). The median (IQR) PASP for patients with and without PH was 41 mm Hg (36–47 mm Hg) and 26 mm Hg (23–29 mm Hg) ($P < 0.001$). Demographics, rates of comorbid illness, and HIV-HCV characteristics were similar between those with and without PH, except a greater proportion of those with PH had been treated for chronic HCV infection (5/9 [56%] vs. 5/27 [19%], respectively;

$P = 0.032$). Among the patients with detailed information about HCV treatment, 16 of 59 (27%) had received therapy, 13 of whom were treated with IFN and ribavirin in combination. One patient who had combination IFN/ribavirin had also received treatment with boceprevir as part of a clinical trial. Three patients had documentation of IFN treatment but no confirmed second agent. We were only able to determine the exact date when HCV treatment concluded in a proportion of patients (5/16 [31%]); in patients in whom this was available, the median interval between date of HCV treatment completion and echocardiogram was 62 months (range, 1–90 mo).

Bivariate and multivariate linear and logistic regression were used to assess the relationship between HIV-HCV risk factors and PASP (as a continuous measure) and PH/RV dysfunction (as a dichotomous measure), respectively. In bivariate analyses, there was no relationship between basic demographics (age, sex, race), drug use or drug type, smoking history, or most HIV-HCV characteristics and other comorbid factors (see Tables E1 and E2 in the online supplement). Time since HCV diagnosis,

the presence of diabetes mellitus, left atrial enlargement, and hemoglobin levels had possible associations with the outcomes of interest ($P < 0.20$), such that these variables were further considered as confounders.

In a multivariable model adjusted for age and sex, there was no relationship between years since HIV diagnosis, control of HIV infection ($CD4^+$ cell count, HIV viral load, and ART), detectable HCV viral load, or SVR and PASP (Table 2). Duration of HCV diagnosis was associated with higher PASP and may have been related to the risk of PH/RV dysfunction (Tables 2–4). A history of HCV treatment was associated with higher PASP and approximately six times the risk of PH/RV dysfunction after adjustment for age and sex. There was a significant association between treatment with IFN specifically and PASP (β , 6.00 mm Hg; 95% confidence interval [CI], 0.09–11.90; $P = 0.047$) and the risk of PH/RV dysfunction (odds ratio [OR], 5.65; 95% CI, 1.07–29.93; $P = 0.042$) after adjustment for age and sex but no relationship between treatment with ribavirin and echocardiographic findings. Although there was no difference in SVR between those with and without PH/RV dysfunction on bivariate analysis ($P = 1.000$), we were unable to test SVR as a predictor in our multivariable model because of the small number of individuals who had definitive documentation of SVR (three total) in the medical record.

The effect estimates between IFN treatment and PASP and PH/RV dysfunction were generally unchanged with sequential adjustment for diabetes mellitus, left atrial enlargement, and hemoglobin (Table 4). Adjustment for years since HCV diagnosis did attenuate the associations between IFN treatment and outcome (β , 3.90 mm Hg; 95% CI, –2.10 to 9.90; $P = 0.194$ for PASP; OR, 4.20; 95% CI, 0.74–23.93; $P = 0.106$ for PH/RV dysfunction). There was no interaction between duration of HCV diagnosis and treatment with IFN and PASP (P for interaction = 0.705) or PH/RV dysfunction ($P = 0.729$).

Discussion

Although the prevalence of PH in HIV monoinfected patients has been well established by hemodynamics at roughly 0.5%, we have demonstrated a 26% prevalence of echocardiographic PH/RV

Figure 1. Study flow. HCV = hepatitis C virus; HIV = human immunodeficiency virus; ICDB = Immunology Center Database; LVEF = left ventricular ejection fraction; PH = pulmonary hypertension; RV = right ventricle.

Table 1. Patient characteristics

Variables	All Patients	No PH	PH	P Value
Number	68	32	11	
Men, n (%)	45 (67)	20 (63)	8 (73)	0.719
Age, yr	52 (48–57)	52 (46–57)	53 (45–57)	0.604
Race/ethnicity, n (%)				1.000
White	36 (53)	17 (53)	7 (64)	
Black	27 (40)	12 (38)	4 (36)	
Asian	1 (1)	1 (3)	0 (0)	
Other	3 (4)	2 (6)	0 (0)	0.874
Smoking history, n (%)				
Current	53 (78)	23 (72)	8 (73)	
Past	8 (12)	5 (16)	1 (9)	
Systemic hypertension, n (%)	26 (38)	12 (38)	4 (36)	1.000
Diabetes mellitus, n (%)	11 (16)	5 (15)	4 (36)	0.152
Airways disease,* n (%)	15 (22)	5 (16)	3 (27)	0.401
Any drug use, n (%)	56/65 (88)	26/30 (87)	8/10 (80)	0.629
Injection drug use, n (%)	39 (57)	19 (59)	7 (64)	0.632
Time since HIV diagnosis, yr	19 (12–24)	18 (12–24)	21 (4–23)	0.532
CD4 ⁺ cell count, k/ μ l	0.45 (0.27–0.66)	0.44 (0.30–0.60)	0.35 (0.19–0.48)	0.625
HIV viral load detectable, n (%)	29 (43)	13 (41)	4 (36)	1.000
ART, n (%)	48 (72)	26 (81)	10 (91)	0.454
Time since HCV diagnosis, yr	8 (5–11)	7 (5–9)	11 (8–12)	0.123
HCV viral load detectable, n (%)	47/66 (72)	22/31 (71)	8/11 (73)	1.000
HCV treated, n (%)	16 (27)	5 (19)	5 (56)	0.032
IFN-based regimen	16/59 (27)	5/27 (19)	5/9 (56)	
HCV, sustained viral response	6 (40)	1 (25)	2 (40)	1.000
Hemoglobin, g/dl	12.8 (11.8–13.9)	12.6 (11.4–13.8)	12.5 (11.9–14.6)	0.116
Creatinine, mg/dl	0.9 (0.7–1.1)	0.9 (0.8–1.2)	0.7 (0.6–0.9)	0.454
Left atrial enlargement, n (%)	16 (25)	6 (18)	4 (36)	0.248
Diastolic dysfunction, n (%)	3 (4)	2 (6)	0 (0)	1.000
PASP, mm Hg	29 (23–36)	26 (23–29)	41 (36–47)	<0.001

Definition of abbreviations: ART = antiretroviral therapy; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IFN = interferon; PASP = pulmonary artery systolic pressure; PH = pulmonary hypertension.

Data are shown as median (interquartile range) or absolute number (%).

*History of asthma, emphysema, or chronic obstructive pulmonary disease.

dysfunction among coinfecting patients without a clinical history of liver disease (3–5). Although many patients had histories of IDU, this did not appear to be a risk

factor for PH or right heart abnormalities, nor were additional markers of HIV-HCV activity. Interestingly, IFN-based HCV treatment was associated with higher PASP

and the risk of PH/RV dysfunction as a dichotomous outcome, but there were no associations between ribavirin and echocardiographic abnormalities, and timing of HCV diagnosis tempered these relationships. To our knowledge, this is one of the larger studies available examining PH in HIV-HCV coinfecting individuals.

The Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy (SUN Study) reported echocardiographic abnormalities in 656 HIV-infected patients, 84 (13%) of whom were coinfecting with HCV (24). Although Mondy and colleagues did not find a significant association between HCV and PH, HIV-HCV coinfection was associated with left ventricular hypertrophy and left ventricular systolic dysfunction (24). In our study, the relationships between IFN treatment and echocardiographic outcomes persisted after adjustment for left atrial enlargement (although precision was poorer), echocardiographic diastolic

Table 2. Associations between estimated pulmonary artery systolic pressure* and baseline human immunodeficiency virus–hepatitis C virus characteristics, adjusted for age and sex

Variable	β	95% CI	P Value
Any drug use	0.67	–7.10 to 8.44	0.862
Injection drug use (current or past)	–0.20	–7.37 to 6.97	0.955
Time since HIV diagnosis, yr	0.02	–0.35 to 0.39	0.918
CD4 ⁺ cell count	–5.05	–15.09 to 4.99	0.315
HIV viral load detectable	–2.94	–9.08 to 3.21	0.339
ART	2.34	–5.36 to 10.04	0.542
Time since HCV diagnosis, yr	0.79	0.08 to 1.50	0.031
HCV viral load detectable	–1.72	–7.89 to 4.45	0.576
HCV treated	6.00	0.09 to 11.90	0.047
IFN treatment	6.00	0.09 to 11.90	0.047
Ribavirin treatment	4.79	–1.47 to 11.05	0.129

Definition of abbreviations: ART = antiretroviral therapy; CI = confidence interval; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IFN = interferon.

*As a continuous measure.

Table 3. Associations between pulmonary hypertension and right ventricular dysfunction (pulmonary artery systolic pressure ≥ 40 mm Hg and/or more than moderate right ventricular dilatation) and baseline human immunodeficiency virus–hepatitis C virus characteristics, adjusted for age and sex

Variable	OR	95% CI	P Value
Any drug use	0.47	0.06–3.81	0.481
Injection drug use (current or past)	0.45	0.04–4.74	0.509
Time since HIV diagnosis, yr	0.97	0.88–1.06	0.520
CD4 ⁺ cell count	0.45	0.03–6.95	0.565
HIV viral load detectable	0.97	0.20–4.66	0.969
ART	2.05	0.20–20.63	0.543
Time since HCV diagnosis, yr	1.21	0.97–1.50	0.097
HCV viral load detectable	1.07	0.23–5.04	0.936
HCV treated	5.65	1.06–29.93	0.042
IFN treatment	5.65	1.07–29.93	0.042
Ribavirin treatment	3.73	0.70–19.90	0.123

Definition of abbreviations: ART = antiretroviral therapy; CI = confidence interval; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IFN = interferon; OR = odds ratio.

dysfunction was rare, and we excluded those with left-sided systolic dysfunction, but we cannot say for certain whether pulmonary venous hypertension contributed to our observations. Another study of 108 HCV monoinfected patients demonstrated a 14% prevalence of echocardiographic PH, although one-third of the patients had portal hypertension in this cohort (25). In patients with advanced liver disease, HCV monoinfection appears to protect against portopulmonary hypertension (26). We excluded patients with known liver disease and studied only coinfecting patients, making comparisons across studies difficult; either of these factors (the cirrhotic state and/or coinfection as opposed to monoinfection) alone or in combination may lead to differential effects on the pulmonary circulation and possibly biventricular function.

How chronic viral infection leads to the development of pulmonary vasculopathy is not known, although several hypotheses exist (6, 27). It has been proposed that chronic HCV infection may induce a type III hypersensitivity reaction, culminating in immune complex deposition and a pulmonary vasculitis (27). Hepatitis B virus stabilizes hypoxia-inducible factor α and leads to the downstream development of PH *in vitro* (6, 28). More recently, Spikes and colleagues demonstrated macaques infected with SIV and injected with morphine have markedly increased pulmonary vascular changes, with increased numbers of apoptosis-resistant cells and advanced plexiform lesions, when compared with morphine-treated, uninfected animals or SIV-infected animals (14). Although in our study IDU was not associated with PASP or PH, it is unknown whether in humans HCV adds

another “hit” to the pulmonary vasculature by acting synergistically with injection drugs and/or HIV infection, especially because HIV-HCV coinfection is frequently transmitted via IDU (15, 29).

Consensus guidelines in pulmonary vascular disease have recently been updated to include IFN as a potential risk factor for drug-induced pulmonary arterial hypertension after case reports emerged of patients treated with IFN- α for HCV and IFN- β for multiple sclerosis (2, 18, 30, 31). PH has also been reported after IFN treatment for chronic myelogenous leukemia and melanoma (32, 33). Our study, although small, supports this concept. Reiberger and colleagues prospectively examined hemodynamic changes in a cohort of coinfecting patients (the majority of whom had concurrent portal hypertension or advanced liver fibrosis) before and after treatment with combination IFN-ribavirin and found no significant changes in pulmonary hemodynamics, although only a subgroup of patients ($n = 31$) had available follow-up measures assessed within a relatively short period of time (6 months) (19). Larger prospective studies of patients treated with IFN have demonstrated decreased diffusing capacity of the lung for carbon monoxide without a significant change in lung volumes that persisted for at least 6 months after therapy, suggesting a direct impact on the pulmonary vascular bed (34, 35). Endothelin-1, a potent pulmonary vasoconstrictor and key mediator in PH, is released from human pulmonary smooth muscle cells when exposed to IFN- α or IFN- γ *in vitro* (17, 36). IFN- α has also been shown to influence the JAK/STAT and thromboxane A2 pathways, both of which

Table 4. Multivariable analysis of the associations between interferon and pulmonary hypertension

Variable	PASP			PH/RV Dysfunction		
	β	95% CI	P Value	OR	95% CI	P Value
Base model*	6.00	0.09 to 11.90	0.047	5.65	1.07 to 29.93	0.042
Adjusted for						
+ Time since HCV diagnosis	3.90	–2.10 to 9.90	0.194	4.20	0.74 to 23.93	0.106
+ Diabetes mellitus	5.86	0.29 to 11.43	0.040	7.98	1.19 to 53.56	0.033
+ Left atrial enlargement [†]	5.94	–0.50 to 12.38	0.069	5.86	0.95 to 36.29	0.057
+ Hemoglobin	7.02	0.62 to 13.43	0.033	4.43	0.75 to 26.04	0.100

Definition of abbreviations: CI = confidence interval; HCV = hepatitis C virus; OR = odds ratio; PASP = pulmonary artery systolic pressure as a continuous measure; PH/RV dysfunction = pulmonary artery systolic pressure ≥ 40 mm Hg and/or more than moderate right ventricular dilatation.

*Adjusted for age and sex.

[†]Defined as a diameter ≥ 3.8 cm in women, ≥ 4.0 cm in men.

have been implicated in pulmonary vascular disease (37, 38). Taken together, larger studies of patients undergoing IFN treatment are necessary to better define this association.

This study has limitations. Our sample was drawn from a larger cohort of patients routinely followed in the Immunology Center (i.e., a highly selected group of patients with respect to follow-up and medical access), and our conclusions may not be generalizable to the HIV-HCV population at large. Ideally we would have compared our coinfecting population to one with HIV monoinfection, but these data were not available. Still, the study sample was similar in baseline characteristics to both the total cohort of coinfecting patients (data not shown) and to those with inadequate echocardiograms (Table 1). The retrospective nature of the study makes it impossible to conclude a causal link between IFN and PH, although patients who had echocardiograms that preceded HCV treatment were excluded. The small sample size limited our ability to adjust for multiple covariates (beyond age, sex, and coexisting comorbidities). The relationships between IFN treatment and echocardiographic outcomes persisted after adjustment for successive potential confounders. Although smoking and drug use did not appear to be associated with PH, detailed substance use histories were not available and we did not have data

on lung function. A sensitivity analysis excluding those with airways disease and diastolic dysfunction, respectively, yielded similar results, although precision was poorer here due to sample size limitations (data not shown).

Right heart catheterization is the gold standard for the diagnosis of pulmonary vascular disease (39). Although echocardiogram is a reasonable noninvasive method of screening for PH, a proportion of our study sample was not included in the final analysis due to either poor acoustic windows or an inadequate tricuspid regurgitant jet to estimate PASP, thus limiting our power and potentially resulting in misclassification of outcome (39). Only two of the patients in the cohort (both of whom were classified as having PH/RV dysfunction) had right heart catheterization performed, confirming pulmonary arterial hypertension (40). Although an echocardiogram-based approach is reasonable as a first step in studying novel risk factors for pulmonary vascular disease, large prospective studies with invasive hemodynamics would be optimal going forward.

We do not have complete data about SVR after HCV treatment or exact dates for completion of HCV therapy and timing of echocardiogram (although all patients had echocardiograms within 6 months of documented HCV infection); for those in whom this was available, timing between

HCV treatment completion and echocardiogram varied widely. This is especially relevant given the relationships noted between time of HCV diagnosis and echocardiographic findings. Although this association is hypothesis generating, it is impossible to conclude that duration of HCV diagnosis was equivalent to duration of HCV infection, especially because we had limited data on SVR from this retrospective cohort. In the small number of individuals with these data available, SVR was not associated with PASP or the risk of PH. Ideally, the relationships between active HCV infection, response to treatment, and potential for relapse as they relate to IFN treatment and possible changes in the pulmonary circulation would be captured.

In this preliminary study, the prevalence of echocardiographic PH in HIV-HCV is substantially higher than that reported for HIV alone. Treatment of HCV with IFN was significantly associated with the development of PH/RV dysfunction, as was duration of HCV diagnosis. Future studies should prospectively define the prevalence of PH in the HIV-HCV coinfecting population and further elucidate potential mechanisms and risk factors for pulmonary vascular disease. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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