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Doppler Echocardiography Does Not Accurately Estimate Pulmonary Artery Systolic Pressure in HIV-Infected Patients

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Keywords

HIV; pulmonary hypertension; Doppler echocardiography; right heart catheterization

Pulmonary arterial hypertension (PAH) is a recognized complication of HIV infection (HIV-related pulmonary arterial hypertension, HRPAH) that is associated with increased mortality[1, 2]. Although right heart catheterization (RHC) is required to definitively diagnose HRPAH, a pulmonary artery systolic pressure (PASP) <35 mmHg estimated by Doppler echocardiography (DE) is a commonly used cutoff to exclude PAH[3]. DE estimates of PASP were recently shown to be inaccurate in a general PAH population, however it is not known if these findings apply to HIV-infected patients[4, 5]. We evaluated the relationship between DE PASP and RHC PASP in a HIV-infected cohort.

We invited HIV-infected individuals enrolled in the SCOPE (Study of the Consequences of the Protease Inhibitor Era) cohort at San Francisco General Hospital to undergo DE. All participants provided written informed consent, and the study was approved by the UCSF Committee on Human Research. DE was performed by a trained sonographer using a GE Vivid 7 system (GE, Milwaukee). Peak tricuspid regurgitant jet velocity was used to calculate the pressure gradient between the right ventricle and right atrium using the modified Bernoulli equation which was added to RA pressure estimated from respiratory variation of the inferior vena cava size to obtain PASP. Because DE-estimated PASP >30 has been associated with increased mortality in patients with sickle cell disease[1], subjects with a DE-estimated PASP > 30 mmHg were offered RHC. RHC was performed using a balloon-tipped, flow-directed pulmonary artery catheter and hemodynamic values were obtained using standard methods.

Analyses were performed using the SAS system, version 9.2 (SAS Institute, Inc., Cary, NC). The relationship of DE-estimated PASP with RHC-measured PASP was examined using Spearman correlation coefficients. The Bland-Altman method was then used to assess the agreement between DE-estimated and RHC-measured PASP. DE-estimated PASP within

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±10 mmHg of the value measured on RHC was considered accurate, consistent with the cutoffs used in other recent publications[4].

Of 422subjects, 129 were found to have PASP > 30 mmHg on DE, 76 of whom consented to undergo RHC. Subjects who underwent RHC were 80% male, had a median age of 52 years (IQR 48 to 56), median duration of HIV infection of 17 years, and 76% were taking antiretroviral therapy. Average PASP estimated on DE was 35.1±11.5 mmHg and the average PASP measured on RHC was 33.9 ± 12.0 mmHg. DE PASP was positively correlated with the RHC PASP ($r=0.49$, $p<0.0001$). Bland-Altman analysis was used to assess the agreement between DE and RHC PASP (Figure 1). The average bias for DE PASP was 1.75 mmHg indicating that DE estimates were on average 1.75 mmHg higher than the RHC measurements; however, the 95% limits of agreement were wide, from −12.0 to 15.5 mmHg. RHC PASP was positively correlated with the difference between the two modalities (DE PASP-RHC PASP) suggesting that the bias increased at higher pressures ($r=0.32$, $p=0.0048$). Overall, DE estimates of PASP were inaccurate (>±10 mmHg different from RHC) in 15 of 76 individuals (19.7%). Fourteen patients received a final diagnosis with PAH. Using the frequently employed threshold of a DE-estimated PASP of ≥ 35 mmHg as abnormal, 5 of the 14, or over 1/3, would have been missed by DE (table 1).

The prevalence of PAH in HIV-infected individuals is 1,000 times higher than in the general population[1, 2] and is expected to increase[6]. Symptoms of HRPAH are non-specific so that appropriate testing is often delayed, and diagnosis with advanced, severe disease is common. Sensitive methods are needed to identify patients who require RHC for definitive diagnosis so that treatment may be initiated promptly[7]. In our cohort DE PASP was, on average, higher than RHC PASP, however limits of agreement were wide. At higher values of PASP, DE was the least accurate and tended to underestimate the RHC-measured PASP so that PASP <35 on DE did not exclude HRPAH.

Our findings are consistent with other recent reports[4, 5]. In a study comparing DE and RHC PASP in 65 PAH patients, the bias for the DE estimates was −0.6 (95% CI +38.8 to −40.0) for RHC and DE was inaccurate in 48% of cases. Although the frequency of under and overestimation of PASP by DE was equal, the magnitude of underestimation was greater[5]. In another study of 142 patients, despite moderate correlation ($r=0.68$, $P< 0.001$), DE PASP was inaccurate in 50.6% of patients with a bias of 2.2 mmHg (95% CI −34.3 to 38.6 mmHg) for DE PASP. Our findings extend upon these other studies, by showing that among individuals with HIV infection DE-estimated PASP is not accurate and relying on DE PASP to exclude a diagnosis of HRPAH could result in missing 1/3 of patients with HRPAH.

Our study is limited because not all subjects consented to undergo RHC and RHC was only performed on subjects with a DE-estimated PASP > 30 mmHg, so the accuracy of DE estimates below this value is uncertain. Additionally, the average PASP in our study was low, 33.9 mmHg, compared to a mean PASP of 68.5 and 57 mmHg in other studies, which could affect our assessment of DE PASP accuracy at higher PASP values. Although we did not perform DE and RHC simultaneously they were performed within one hour of each other and prior reports have confirmed that simultaneous DE and RHC do not improve DE estimation of PASP[4]. We did not account for echocardiographic findings such as right heart size, thickness and function which could modify clinical suspicion for PAH.

Although other DE findings can raise or reinforce suspicion for PAH, major society guidelines consistently emphasize the importance of non-invasive DE estimate of PASP in cases of suspected PAH[3, 8]. In this study, we show for the first time in HIV- infected patients at risk for HRPAH that DE estimates of PASP are not accurate and using a DE

PASP cutoff of >35 mmHg may miss patients with HRPAH . Because HRPAH is associated with high mortality and early and treatment could improve outcome, timely and accurate diagnosis is critical. RHC should be considered in HIV- infected patients with symptoms concerning for HRPAH, even if DE-estimated PASP is not >35 mmHg.

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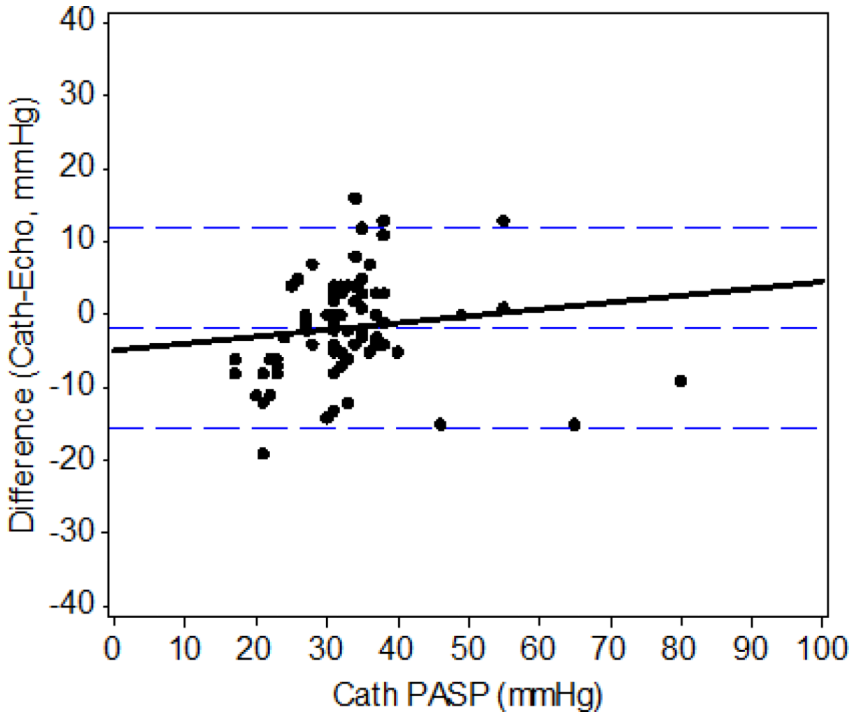

Figure 1.
Bland-Altman analysis demonstrating lack of agreement between the Doppler echocardiogram estimated pulmonary artery systolic pressure (PASP) and right heart catheterization measured PASP.

Table 1

Comparison of Doppler echocardiography (DE) estimated pulmonary artery systolic pressure (PASP) and right heart catheterization measured PASP in patients with a final diagnosis of pulmonary arterial hypertension (PAH) (mean pulmonary artery pressure ≥25 mmHg on right heart catheterization (RHC)). Diagnosis of PAH would have been missed in patients 1-5 using a commonly DE estimated PASP cutoff of <35 mmHg to exclude the diagnosis. All 15 patients had a final diagnosis of PAH with a mean pulmonary artery pressure ≥25 mmHg

Patient	DE PASP (mmHg)	RHC PASP (mmHg)
1	23	35
2	25	38
3	26	34
4	29	31
5	32	34
6	42	38
7	42	55
8	45	40
9	49	49
10	54	55
11	59	95
12	61	46
13	80	65
14	89	80