#### Prevalence of Abnormal Echocardiographic Findings in Thai HIV-infected and Noninfected Aging Population After Receiving Therapy: ECHO THAI-HAART Study

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## Background

In the highly active antiretroviral therapy (HAART) era, cardiovascular disease is the leading problem in HIV-infected individuals. Various abnormal echocardiographic findings included diastolic dysfunction have been reported in this population.<sup>1-3</sup> Little data was known in Thai aging population.<sup>4,5</sup>

### Results

PI-based
NNRTI-based
NRTI-based
Other

# Objectives

To study the **prevalence** of echocardiographic abnormalities in asymptomatic, virally suppressed HIV-infected Thai aging individuals in comparison with non HIV-infected control.

# Methods

- Cross-sectional, observational study.
- Control selection using quota sampling based on age and gender.
- 398 participants (298 [75%], HIV-infected patients) without known cardiovascular disease were enrolled.
- Standard comprehensive 2-dimensional transthoracic echocardiography was interpreted by single experienced reader blinded to the study.

## Results

In HIV-infected patients, a median CD4 count was 614 cell/mm<sup>3</sup> with 16.2 years of HAART exposure. Of these, there were 1.1% with LVEF < 50%, 22.4% with diastolic dysfunction, and 3.2% with pulmonary hypertension (mean PAP  $\ge$  25



100

80

mmHg), **not significantly different** from non HIV-infected patients. Age > 60 years, body mass index > 23 kg/m<sup>2</sup>, hypertension, diabetes and metabolic syndrome were associated with diastolic dysfunction while female, statin exposure and LAVI > 34 mL/m<sup>2</sup> were associated with pulmonary hypertension, p < 0.05.

Table 1 : Demographic data (n=398)							
	All $(n = 398)$	HIV infected $(n = 298)$	Healthy control $(n = 100)$	p-value			
Male	273 (68.6)	209 (70.1)	64 (64)	0.96			
Age, year	55 (22-59)	54.3 (51.7-59.0)	55.4 (52.9-57.8)	0.31			
BMI, kg/m <sup>2</sup>	24 (21-26)	23.3 (20.8-25.4)	25.4 (22.5-28.9)	< 0.001			
Smoking	51 (12.8)	40 (13.4)	11 (11)	0.81			
Diabetes	66 (16.6)	51 (17.1)	15 (15)	0.62			
Hypertension	148 (37.2)	121 (40.6)	27 (27)	0.02			
Metabolic syndrome	162 (40.7)	124 (41.6)	38 (38)	0.53			
Current statin use	130 (32.7)	111 (37.3)	19 (19)	<0.001			
CD4, cell/mm <sup>3</sup>		614 (485-804)	NA				
HIV-RNA < 50 copies/mL		290 (97.4)	NA				
HAART Exposure, years		16.2 (12.5-25.8)	NA				
Abacavir exposure		25 (8.4)	NA				
Creatinine, mg/dL	1.0 (0.7-1.05)	0.87 (0.76-1.05)	0.85 (0.73-0.95)	0.05			
Fasting plasma glucose, mg/dL	93 (85-102)	93 (85-102)	94 (86-104)	0.49			
Total cholesterol, mg/dL	210 (183-238)	205 (179-238)	220 (196-244)	0.007			
Triglycerides, mg/dL	141.5 (98-203)	153 (105-216)	122 (93-168)	<0.001			
LDL, mg/dL	127.5 (104-152)	125 (102-149)	140 (117-161)	<0.001			
HDL,mg/dL	49 (40-57)	46 (39-57)	51 (44-60)	< 0.001			
Interleukin-6, pg/mL	6 (4-9)	5.93 (4.14-8.17)	6.29 (4-11.67)	0.36			
hs-CRP, mg/L	1 (1-3)	1.21 (0.59-2.67)	1.32 (0.49-2.76)	0.933			
hs-CRP > 2 mg/L	176 (44.2)	131 (43.96)	45 (45)	0.22			
ABI	1.0 (1.0-1.0)	1.07 (1.04-1.12)	1.07 (1.02-1.12)	0.99			
CAVI (Cardio-ankle vascular index)	8 (7-9)	7.7 (7.2-8.7)	7.6 (7.1-8.4)	0.09			

Gender			Age group				
	Male	Female	50-59	60-69	70		

**Figure 3**: Distribution of LVEF, LV mass index, mPAP and average E/e' between HIV infected and non-HIV infected groups.

**Figure 4:** Distribution of diastolic dysfunction between HIV infected and non-HIV infected groups.

74.3

Factors	Odds ratio	95% CI	P-value							
	Diastolic dysfund	ction								
Age > 60 years	4.27	(2.36-7.72)	< 0.001	Variables	Univa	ariate Analysi	S	Multiv	<i>r</i> ariate Analys	is
$BMI > 23 \text{ kg/m}^2$	2.07	(1.19-3.62)	0.01		Coefficience	95%CI	p-value	Coefficience	95%CI	p-va
Hypertension	3.6	(1.80-7.22)	< 0.001	Age	0.09	(0.04, 0.15)	< 0.001	0.02	(-0.04, 0.08)	0.4
Diabetes	1.93	(1.05-3.52)	0.03	BMI	0.15	(0.21, 1.3) (0.08, 0.23)	< 0.008	0.12	(0.74, 1.91) (0.04.0.21)	< 0.0
Metabolic syndrome	3.1	(1.79-5.37)	< 0.001	HT	0.84	(0.26, 1.41)	0.004	0.56	(05,1.16)	0.0
hs-CRP > 2 mg/L	1.03	(0.60-1.75)	0.92	LV Mass	0.02	(0.01, 0.03)	< 0.001	0.02	(0,01,0,03)	< 0 (
High ASCVD risk	2.15	(1.26-3.69)	0.005	index	0.02	(0.01, 0.03)	<0.001	0.02	(0.01,0.03)	<0.c
Intermediate-to-high ASCVD risk	2.06	(1.15-3.70)	0.01	hs-CRP > 2 mcg/L	0.59	(-0.01, 1.2)	0.053	0.51	(07,1.08)	0.0
	Pulmonary hyperte	ension		LDL-C	0.01	(-0.001,0.01	0.09	0.01	(002, 0.01)	0.1
Female	4.2	(1.09-16.2)	0.04	CAVI	0.33	(0.1, 0.57)	0.006	0.35	(0.11,0.59)	0.0
Statin exposure	4.38	(1.25-15.4)	0.02							
$LAVI > 34 \text{ mL/m}^2$	6.45	(1.86-22.4)	0.003							

**Table 3**: Factors associated with LV diastolic dysfunction andpulmonary hypertension in HIV-infected patients.

**Table 4**: Univariate and multivariate regression analysis of factorsassociated with average E/e' in HIV-infected group.

	LV systolic dysfunction			LV diastolic dysfunction			Pulmonary hypertension		
	N = 2			N = 72			N = 11		
Antiretrovirus	Odds ratio	95% CI	p- value	Odds ratio	95% CI	p- value	Odds ratio	95% CI	p- value
Abacavir $n = 25$	2.13	(0.10-45.6)	0.63	1.88	(0.79-4.45)	0.15	2.66	(0.54-13.1)	0.23
Lopinavir n = 129	1.77	(0.08-37.2)	0.71	1.06	(0.62-1.81)	0.82	0.48	(0.12-1.84)	0.28
Atazanavir n = $94$	11.05	(0.53-23.2)	0.12	1.21	(0.69-2.12)	0.51	1.26	(0.36-4.43)	0.71
Other boosted PI $n = 221$	0.94	(0.24-3.63)	0.93	1.17	(0.63-2.17)	0.62	0.94	(0.24-3.63)	0.93
Efavirenz n = $177$	0.68	(0.42-11.0)	0.79	0.75	(0.44-1.28)	0.3	0.46	(0.12-1.80)	0.26
Stavudine (D4T) $n = 185$	0.61	(0.38-9.83)	0.72	1.41	(0.80-2.47)	0.23	1.67	(0.43-6.42)	0.46
Tenofovir $n = 254$	0.88	(0.04-18.7)	0.93	0.95	(0.45-1.99)	0.88	0.95	(0.45-1.99)	0.88
Zidovudine (AZT) $n = 28$	2.33	(0.11-49.9)	0.59	1.12	(0.42-2.95)	0.82	2.81	(0.57-13.9)	0.21
Indinavir $n = 84$	2.57	(0.16-41.5)	0.49	1.27	(0.71-2.26)	0.42	0.55	(0.12-2.63)	0.46

#### Values are Number(%), Median (p25-75)

Table 2: Echocardiographic results by HIV group (n=398)								
	All	HIV-infected	Control	1				
	(n=398)	(n=298)	(n=100)	p-value				
LV ejection fraction, %	68 (62-72)	67.4 (61.4-72.1)	68.3 (62-72.9)	0.43				
LV Mass Index (female), g/m <sup>2</sup>	92 (75.5-106.5)	88.6 (75.9-106.7)	96.1 (65.2-111)	0.94				
LV Mass Index (male), g/m <sup>2</sup>	109 (89-123)	105.1 (89.4-122.8)	103.9 (89-127.5)	0.94				
LAVI, mL/m <sup>2</sup>	24 (19-30)	23.5 (186-29.7)	24 (18.8-30.6)	0.49				
E/A ratio	1 (1-1)	0.98 (0.81-1.18)	0.94 (0.78-1.15)	0.21				
Medial e', cm/s	7 (6-8)	7.2 (6-8.4)	7 (5.95-8.2)	0.69				
Lateral e', cm/s, n=387	10 (8-11)	9.3 (7.9-10.8)	9.75 (8.15-11.2)	0.12				
Average E/e'	10 (8-12)	8.7 (7.4-10.4)	8.5 (7.4-10.1)	0.40				
TAPSE, mm, n=396	23 (20-25)	22 (20-25)	23 (20-25)	0.95				
RVSP, mmHg, n=348	28 (24-32)	28 (23.5-32.1)	26.7 (23.8-30.3)	0.44				
mPAP, mmHg, n=324	19 (17-21)	18.8 (17.1-21.3)	18.3 (16-20.7)	0.07				

Values are Median (p25-75) LV: left ventricle, LAVI: left atrial volume index, TAPSE: tricuspid annular plane systolic excursion, RVSP: right ventricular systolic pressure, mPAP: mean pulmonary artery pressure

**Table 5**: Association between antiretroviral drugs and LV systolic dysfunction, LV diastolicdysfunction, and pulmonary hypertension.

#### Conclusions

In this large echocardiographic study in well-treated, virally suppressed aging HIVinfected population, the prevalence of asymptomatic left ventricular systolic dysfunction and pulmonary hypertension were low.

In the new HAART era, the prevalence of structural cardiac abnormalities in HIVinfected patients were not different from age and gender-based quota sampling control.

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