A comparison of the risk for cardiovascular disease between HIV-infected and non-HIV-infected persons in Korea

Sun Bean Kim

Department of Medicine

The Graduate School, Yonsei University

A comparison of the risk for cardiovascular disease between HIV-infected and non-HIV-infected persons in Korea

Directed by Professor June Myung Kim

The Master's Thesis
submitted to the Department of Medicine of
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the
degree of Master of Medical Science

Sun Bean Kim

June 2012

This certifies that the Master's Thesis of Sun Bean Kim is approved.

Thesis Supervisor: June Myung Kim

Thesis Committee Member#1: Bong Su Cha

Thesis Committee Member#2: Jae Myun Lee

The Graduate School

Yonsei University

June 2012

ACKNOWLEDGEMENTS

I would like to express my gratitude to all those who gave me the possibility to complete this thesis. Most of all, I want to thank Dr. June Myung Kim as my great adviser. I also want to thank Dr. Jun Yong Choi and Sang Hoon Han as my good tutors. I always feel lucky to have you as my good teachers. I also would like to thank Dr. Bong-su Cha and Jae-Myun Lee, who were my good consultants. In addition, I would like to thank my co-workers, Nam-su Ku, Su Jin Jeong, and Hye-won Kim, because you're always inspiring me. I also would like to express my gratitude to old my friends, Dong-hyeon Gu, Duck-Jin Hong, and especially Hyun-june Lee as my good supporter.

I would like to express my highest gratitude to my parents, who are my root of life. I really respect and love you. I also would like to thank my only brother, sister-in-law, and two lovely nieces (Hye-Min and Hye-Yoon). I really love all of you.

<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

<ABSTRACT>

A Comparison of the risk for cardiovascular disease between HIV-infected and non-HIV-infected persons in Korea.

Sun Bean Kim

Department of Medicine or Medical Science
The Graduate School, Yonsei University

(Directed by Professor June Myung Kim)

Background:

Cardiovascular disease (CVD) is the most common cause of death worldwide. The introduction of highly active anti-retroviral therapy (HAART) has improved the quality of life and expanded the life expectancy of persons infected with human immunodeficiency virus type 1 (HIV-1). However, CVD is currently an increasing concern for HIV-infected persons and risk assessment is recommended as part of HIV patient care. Risk prediction tools such as the Framingham Risk Score (FRS) have been developed to identify patients at high CVD risk who may require therapeutic interventions. A number of articles have appeared regarding cardiovascular (CV) risk factors in HIV-infected persons who are naïve or treated with HAART. However, only a few publications have compared the risk factors for HIV-infected and non-HIV-infected persons(a healthy control group) in Korea.

Methods:

This study was designed as a cross-sectional study and was conducted at an outpatient clinic at the Severance Hospital, Yonsei University College of Medicine, and the Health Care Center of Yonsei Medical Center. The study investigated HIV-infected persons (N=116) who had been receiving HAART for more than 6 months and compared them to non-HIV-infected persons(a healthy control group) selected from age- and sex-matched persons who visited a health promotion center for periodic medical checkups (N=226). The aim of this study was to evaluate and compare the CV risk of HIV-infected and non-HIV-infected persons by calculating the Framingham Risk Scores (FRS).

Results:

The HIV-infected persons and non-HIV-infected persons (a healthy control group) did not differ by age (p=0.43) or gender (p=0.47). The HIV-infected persons had significantly higher levels of serum triglycerides, LDL cholesterol, and systolic blood pressure ($p < 0.0001$). The average 10-year risk for CV events (determined by FRS) was 7.07% (2-45) in the HIV-infected persons and 6.87% (1-37) in the non-HIV-infected persons (a healthy control group)(p= 0.77); both belonged to the very low risk group.

Among HIV-infected persons, the FRS indicated low to moderate cardiovascular risk in 19.9 %, and high risk in 1.7%. In the non-HIV-infected persons, the FRS indicated low to moderate cardiovascular risk in 16.8%, and high risk in 2.7%(p = 0.57). No

statistically significant effect on FRS was found for the HAART regimen, especially non-nucleoside reverse transcriptase inhibitor-based (NNRTI -based) (6.81 ± 4.4) versus protease inhibitor-based (PI-based) (7.26 ± 6.3) regimens (p=0.69).

Conclusion:

Approximately 70% of HIV infected persons were categorized into a low cardiovascular risk group. In addition, the 10-year cardiovascular risk prediction between HIV infected and non-HIV-infected persons was not significantly different (p=0.57). Based on these results, a long-term prospective cohort study for detecting the cardiovascular risks for HIV infected persons is considered.

Key words：Framingham Risk score; HIV; HIV infection; HAART; Healthy control group

A comparison of the risk for cardiovascular disease between HIV-infected and non-HIV-infected persons in Korea.

Sun Bean Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor June Myung Kim)

I. INTRODUCTION

Cardiovascular disease (CVD) is the most common cause of death worldwide and is now a concern among patients infected with human immunodeficiency virus (HIV). Infection with HIV continues to increase globally; in Korea, the total number is about 8,000 people since the first HIV-infected person was found in 1985. In the early days of the HIV epidemic, survival was rare. The introduction of highly active anti-retroviral therapy (HAART) has since improved the quality of life and expanded the life expectancy for human immunodeficiency virus type 1 (HIV-1)-infected persons[1]. Prior to 1996, the annual mortality rate among HIV-1 infected persons exceeded 20 percent; after a decade of effective treatment, annual mortality has declined to less than 2 percent[2]. However, HIV is not a curable disease and infected persons require treatment for their entire lives[1]. The longer patient survival, has sparked new interest regarding the side effects of prolonged use of combination antiretroviral therapy (ART), including increased fat redistribution, lipoatrophy, fat accumulation, or a combination of these features[3,4]. In addition to changes in fat

distribution, other metabolic abnormalities are observed in patients on combination ART, including dyslipidemia, diabetes mellitus, and insulin resistance[5].

Currently, CVD is an increasing concern for HIV-infected persons and risk assessment is recommended in their care[6,7]. Risk prediction tools such as the Framingham Risk Score (FRS) have been developed to identify persons at high risk who may require therapeutic interventions. The variables measured in the FRS include age, sex, smoking status, diabetes status, cholesterol levels, and blood pressure values[8]. This type of information allows clinicians to use gender-specific risk score tables in assigning points that can be translated into a specific 10-year cardiovascular risk [8].

The purpose of risk stratification is to provide a simple way to verify and treat HIV-infected persons who may be at higher long-term cardiovascular (CV) risk. The FRS has been validated in many different populations and ethnic groups and recalibrated appropriately[9-12], making it a well-known risk index that allows comparison of risks across different population groups. Previous investigators[13,14] have evaluated the CV risk in patients with HIV infection by calculating FRS; however, a few associated reports have compared the CV risk of HIV-infected persons with that of non-HIV infected persons. The results of other studies concerning the prevalence of CVD (especially in western cohorts) in HIV-infected persons may also differ from results in East Asia, including Korea[15]. This difference is thought to be due to the prevalence of HIV infection and types of HAART regimens and the traditional risk factors including age, sex, smoking history, hypertension and body mass index (BMI)[15].

The aim of this study is to evaluate and compare the CV risk of HIV-infected and non-HIV-infected (a healthy control group) Korean by calculating their respective FRS.

II. MATERIALS AND METHODS

1. Study population and cardiovascular risk assessment

A. Study population

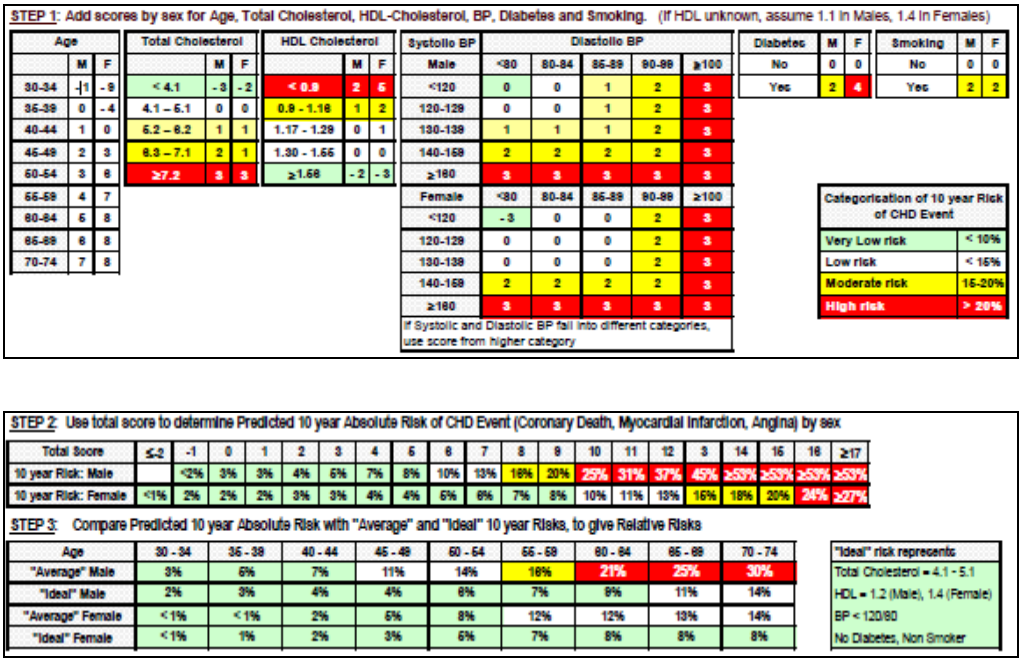
This study was designed as a cross-sectional study and conducted at an outpatient clinic in Severance Hospital, Yonsei University College of Medicine, where HIV infected persons (N=116) were selected who were regularly visiting the division of infection every three months and who had been receiving HAART for more than 6 months. Their metabolic profiles at initial HIV status (Naïve) were studied retrospectively. Non-HIV-infected persons (N=226) were selected from age- and sex-matched persons as a control group and were a generally healthy population. All eligible persons were older than 30 year of age. To prevent overestimating or underestimating the predicted cardiovascular risk due to overt cardiovascular disease and medication, any HIV-infected persons who had prior CVD history, were taking anti-hypertensive or diabetes medication, or had undergone treatment for opportunistic infection were excluded. All enrolled persons were evaluated for metabolic profiles; blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, fasting glucose and body composition. Based on these variables, their 10-yr cardiovascular risk was predicted by calculating a Framingham Risk Score (FRS). HIV-infected persons were further evaluated for additional information including the duration of HIV infection, CD4+ T lymphocyte count, titer of HIV-RNA, and duration/types of HAART to identify the relationship between these values and the cardiovascular risk score.

B. Cardiovascular risk assessment

(A) Calculation of cardiovascular disease risk using the Framingham equation

The Framingham equation can only be used to calculate CV risk in the absence of CVD (primary prevention), but may be used in both men and women. The following variables were considered: age, gender, systolic and diastolic blood pressure, serum total cholesterol levels, HDL-cholesterol level, the presence/absence of diabetes, and smoking status. Subjects were classified as having very low, low, moderate, or high 10-year coronary risk in accordance with the Framingham equation (<10%, 10-15%, 16-20%, and >20%, respectively)[16]. The FRS was calculated for all persons using a composite-simplified coronary prediction model built on blood pressure and cholesterol categories, as suggested by the Joint National Committee on Blood Pressure and the National Cholesterol Education Program[17]. Among the variables of the FRS, presence/absence of diabetes was confirmed by checking a fasting glucose level (above 126mg/dL indicating diabetes) according to the American Diabetes Association guidelines[18].

Fig 1. Calculation of the Framingham Risk Scores(FRS).



STEP 1: Add scores by sex for Age, Total Cholesterol, HDL-Cholesterol, BP, Diabetes and Smoking. (If HDL unknown, assume 1.1 in Males, 1.4 in Females)

Age	M	F
30-34	-1	- 9
35-39	0	- 4
40-44	1	0
45-49	2	3
50-54	3	6
55-59	4	7
60-64	5	8
65-69	6	8
70-74	7	8

Total Cholesterol	M	F
< 4.1	- 3	- 2
4.1 – 5.1	0	0
5.2 – 6.2	1	1
6.3 – 7.1	2	1
≥7.2	3	3

HDL Cholesterol	M	F
< 0.9	2	5
0.9 - 1.16	1	2
1.17 - 1.29	0	1
1.30 - 1.55	0	0
≥1.56	- 2	- 3

Systolic BP	Diastolic BP				
Male	<80	80-84	85-89	90-99	≥100
<120	0	0	1	2	3
120-129	0	0	1	2	3
130-139	1	1	1	2	3
140-159	2	2	2	2	3
≥160	3	3	3	3	3
Female	<80	80-84	85-89	90-99	≥100
<120	- 3	0	0	2	3
120-129	0	0	0	2	3
130-139	0	0	0	2	3
140-159	2	2	2	2	3
≥160	3	3	3	3	3

If Systolic and Diastolic BP fall into different categories, use score from higher category

Diabetes	M	F
No	0	0
Yes	2	4

Smoking	M	F
No	0	0
Yes	2	2

Categorication of 10 year Rick of CHD Event	
Very Low rick	< 10%
Low risk	< 15%
Moderate rick	15-20%
High risk	> 20%

STEP 2: Use total score to determine Predicted 10 year Absolute Risk of CHD Event (Coronary Death, Myocardial Infarction, Anginaj by sex

Total Score	≤-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	≥17
10 year Rick: Male		<2%	3%	3%	4%	5%	7%	8%	10%	13%	16%	20%	25%	31%	37%	45%	≥53%	≥53%	≥53%	≥53%
10 year Rick: Female	<1%	2%	2%	2%	3%	3%	4%	4%	5%	6%	7%	8%	10%	11%	13%	16%	18%	20%	24%	≥27%

STEP 3: Compare Predicted 10 year Absolute Risk with "Average" and "Ideal" 10 year Risks, to give Relative Risks

Age	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65 - 69	70 - 74
"Average" Male	3%	5%	7%	11%	14%	16%	21%	25%	30%
"Ideal" Male	2%	3%	4%	4%	6%	7%	9%	11%	14%
"Average" Female	< 1%	< 1%	2%	5%	8%	12%	12%	13%	14%
"Ideal" Female	< 1%	1%	2%	3%	5%	7%	8%	8%	8%

"Ideal" risk represents
Total Cholesterol = 4.1 - 5.1
HDL = 1.2 (Male), 1.4 (Female)
BP < 120/80
No Diabetes, Non Smoker

C. Statistical analysis

Data were analyzed using the Statistical Package for SAS version. (9.1.3, SAS institute Inc., Cary, NC, USA) Quantitative variables were presented as means ± standard deviations or medians with their respective 95% confidence intervals, according to their distribution. Categorial variables were presented as percentages. Between-group differences in the percentages for categorical variables were evaluated by a Pearson Chi test. Student's t-tests were used to assess the differences in normally and non-normally distributed variables. Non-normal variables were log-transformed before analysis.

III. RESULTS

A total of 116 HIV-infected persons and 226 non-HIV-infected persons were analyzed. There were 113 men and 3 women among the HIV-infected persons and 215 men and 11 women in non-HIV-infected persons. The metabolic profiles of HIV-infected persons were evaluated at the time of their first visit (Naïve status) and when FRS values were determined (FRS calculation) (Table 1).

Table 1. Baseline Characteristics of HIV-infected persons (Naïve vs HAART treated)

Variables	At the time of HIV diagnosis (Naïve)	At the measurement of FRS (HAART treated)	*P*-value
Age (years)	37 ± 9	41.9 ± 8.9	0.38
Gender, male	114 (98%)	114 (98%)	1.0
Elapsed time since HIV diagnosis (months)		56. 8 (50-202)	
Duration of HAART (months)		37.9 (15-126)	
CD 4+ T lymphocytes count (/μL)	220.4 ± 162.6	462.8 ± 240.9	< 0.001
Plasma HIV-RNA Viral load (Log[copies/ml])	4.56 ± 1.2	1.75 ± 0.52	0.001
Metabolic profile			
Fasting glucose (mg/dL)	100.1 ± 27	97.7 ± 18	0.405
Total cholesterol (mg/dL)	146.6 ± 32.3	186.6 ± 40.7	< 0.001
HDL-cholesterol (mg/dL)	37.3 ± 10.8	46.7 ± 11.5	< 0.001
LDL-cholesterol (mg/dL)	82.6 ± 24.7	88.9 ± 34.9	0.007
Triglyceride (mg/dL)	154.5 ± 68.9	266.2 ± 200.4	< 0.001
Blood pressure (mmHg)			
Systolic	123.3 ± 18.9	122 ± 11.7	0.61
Diastolic	80.5 ± 7.8	83.5 ± 10.2	0.267

Data were expressed the mean ± SD or number (percent).

All of the enrolled HIV-infected persons were treated with HAART. The median duration of HIV diagnosis was 56.8 months and HAART duration was 37.9 months. The median age at the naïve analysis and at FRS calculation was 37 and 42 yrs, respectively. The median CD4+ T lymphocyte count was 220 /μL at naïve status and 462 /μL at FRS calculation (p <0.0001). The median titer of plasma HIV RNA viral load (Log[copies/ml]) was 4.56 at naïve status and 1.75 at FRS calculation (p <0.0001). Metabolic profiles including blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were significantly higher (p <0.0001) at FRS calculation than at naïve status, but blood pressure and fasting glucose levels were not statistically different. The differences in blood lipids appeared to be associated with HAART (Table 1). The HAART regimens and duration of treatment are shown in Table 2.

Table 2. Combined antiretroviral treatment of HIV-infected persons.

Variables	
cART regimen at the measurement of FRS	N (%)
NNRTI-based	40/116 (34)
PI-based	76/116 (66)
Boosted PI	51/76 (67)
Unboosted PI	25/76 (33)
Use of PI during more than 6 months, yes	75/76 (99)
Use of thymidine analogues (AZT or d4T or ddI during more than 6 months, yes)	106/116 (91)
Total duration of cART (months)	37.8 ± 29.5
Total duration of NNRTI-based cART (months)	25.7 ± 23.3
Total duration of PI-based cART (months)	28.8 (1.2-122)
Total exposure duration of d4T (months)	42.2 ± 27.8
Total exposure duration of ddI(months)	21.3 (1.5-114)
Total exposure duration of Lopinavir/Ritonavir (months)	27.6 (1.2-114)

Data were expressed the mean ± SD or number (percent).

An effect of HIV infection itself on metabolic profiles was confirmed by evaluation of the baseline characteristics of initial HIV-infected persons (naïve status) compared to non-HIV-infected persons (Table 3.). No significant differences were found for age, gender, triglycerides, or blood pressure. However, significant differences were found for cholesterol levels (total, HDL, and LDL cholesterol).

Table 3. Baseline characteristics of HIV-infected persons (Naïve) and non-HIV-infected persons (a healthy control group).

Variables	Case group (Naïve) (N=116)	Control group (N=226)	*P*-value
Age (years)	37 ± 9	42 ± 9	0.332
Gender, male	114 (98)	198 (96)	0.472
Metabolic profile			
Total cholesterol (mg/dL)	123.3 ± 18.9	196.7 ± 34.1	< 0.001
HDL-cholesterol (mg/dL)	37.3 ± 10.8	50± 12.3	< 0.001
LDL-cholesterol (mg/dL)	82.6 ± 24.7	120.5 ± 30.2	< 0.001
Triglyceride (mg/dL)	154.5 ± 68.9	151.7 ± 96.3	0.806
Blood pressure (mmHg)			
Systolic	123.3 ± 18.9	122 ± 11.7	0.839
Diastolic	80.5 ± 7.9	83.5 ± 10.2	0.560

Data were expressed the mean ± SD or number (percent).
Case group : "HIV-infected persons (Naïve status)"
Control group : "Non-HIV-infected persons (A healthy control group)"

Differences in FRS between HIV-infected persons and non-HIV-infected persons were calculated. Because the groups were matched, HIV-infected and non-HIV-infected persons did not differ by age (p=0.43) or gender (p=0.47). No significant differences were found for smoking (p=0.35). The HIV group had significantly higher levels of serum triglycerides, LDL cholesterol, and systolic blood pressure ($p < 0.0001$). However, body component measurements including waist circumference, waist-height ratio (WHR) and BMI were higher in the non-HIV-infected persons than in the HIV-infected persons ($p< 0.001$) (Table 4.).

Table 4. Baseline characteristics of HIV-infected persons (at the measurement of FRS) and non-HIV-infected persons (a healthy control group).

Variables	**Case group (N=116)**	**Control group (N=226)**	***P*-value**
Age (years)	41.9 ± 8.8	42 ± 9	0.957
Gender, male	114 (98%)	198 (96%)	0.472
Metabolic profile			
Total cholesterol (mg/dL)	186.6 ± 40.7	196.7 ± 34.2	0.023
HDL-cholesterol (mg/dL)	46.7 ± 11.5	50 ± 12.3	0.019
LDL-cholesterol (mg/dL)	88.9 ± 34.9	120.5 ± 30.2	< 0.001
Triglyceride (mg/dL)	266.2 ± 200.4	151.8 ± 96.3	< 0.001
Fasting glucose (mg/dL)	97.7 ± 17.9	94.2 ± 19.2	0.107
Smoking , yes (%)	87 (74.3)	162 (71.7)	0.357
Blood pressure (mmHg)			
Systolic	129.8 ± 14.8	122 ± 11.7	< 0.001
Diastolic	78.2 ± 11.3	83.5 ± 10.2	< 0.001
Total value of FRS (point)	7.07 (2-45)	6.87 (1-37)	0.769
Body composition			
Waist circumference (cm)	82.7 ± 6.9	86.3 ± 8.3	< 0.001
WHR	0.87 ± 0.1	0.89 ± 0.34	< 0.001
BMI (kg/m^2)	22.8 ± 2.7	24.8 ± 3.2	< 0.001

Data were expressed the mean ± SD or median (interquartile range) or number (percent).
Case group **: "**HIV-infected persons (at the measurement of FRS)"
Control group : "Non-HIV-infected persons(a healthy control group)"

The average 10-year risk for cardiovascular events (FRS) was 7.07% (2-45) in HIV-infected persons and 6.87% (1-37) in the non-HIV-infected persons (p= 0.76). Among the HIV-infected persons, the FRS indicated low to moderate cardiovascular risk in 19.9 %, and high risk in 1.7 %. In the non-HIV-infected persons, the FRS indicated low to moderate cardiovascular risk in 16.8%, and high risk in 2.7%(p = 0.78). In addition, after categorizing into four groups (very low risk, low risk, moderate risk, and high risk) by scoring the risk factors, no significant difference was found among the groups (p= 0.57) (Table 5.).

Table 5. Comparisons of 10-year risk of coronary heart disease events based on Framingham Risk Score (FRS).

Categories	**Case group (N=116)**	**Control group (N=226)**	***P*-value**
Very low risk	82 (70.7)	182 (80.5)	
Low risk	17 (14.7)	24 (10.6)	
Moderate risk	6 (5.2)	14 (6.2)	
High risk	2 (1.7)	6 (2.7)	
			0.78

Data were expressed the Number and percentage.
Case group **: "**HIV-infected persons (at the measurement of FRS)"
Control group : "Non-HIV-infected persons (A healthy control group)"

The HAART regimen, especially NNRTI-based (6.81 ± 4.4) versus PI-based (7.26 ± 6.3) regimens, had no significant effect on FRS ($p = 0.69$). Moreover, the components of the metabolic profile, including blood pressure, lipid profile, and body composition, were not significantly different (systolic blood pressure, $p = 0.603$; diastolic blood pressure, $p = 0.248$; total cholesterol, $p = 0.433$; LDL-cholesterol, $p = 0.098$; Triglyceride, $p = 0.102$,; fasting glucose, $p = 0.21$; WHR, $p = 0.25$)(Table 6.).

Table 6. Association between antiretroviral regimen and metabolic profiles.

	HAART regimen		
	NNRTI based (N=40)	PI based (N=76)	P-value
Blood pressure (mmHg)			
Systolic (mmHg)	128.8 ± 15.8	130.3±14.7	0.603
Diastolic(mmHg)	76.3 ± 11.7	78.9 ± 11.3	0.248
Metabolic profile			
Total cholesterol (mg/dL)	189.4 ± 41.6	183.2 ± 40.3	0.433
HDL-cholesterol (mg/dL)	48 ± 10.9	45.7 ± 11.9	0.311
LDL-cholesterol (mg/dL)	95.1 ± 42.3	83.8 ± 28.9	0.098
Triglyceride (mg/dL)	225.7 ± 137	290.3 ±223.3	0.102
Fasting glucose (mg/dL)	100.3±20.6	95.9 ± 15.9	0.21
Total value of FRS (point)	6.81 ± 4.4	7.26 ± 6.3	0.699
Body composition			
Waist circumference (cm)	82.4 ± 6.8	82.9 ± 7.1	0.749
WHR	0.87± 0.04	0.88± 0.05	0.25
BMI (kg/m^2)	23.1± 2.9	22.7 ± 2.6	0.406

Data were expressed the mean ± SD or number (percent).

IV.DISCUSSION

Cardiovascular disease is an important concern in HIV-infected persons treated with HAART, due to the occurrence of adverse dyslipidemic effects[4]. Even before the era of HAART, investigators noticed that untreated HIV-infected (Naïve) persons had altered lipid profiles, including lowered HDL and LDL cholesterol levels, and elevated triglyceride levels[19,20]. With the widespread use of HAART, the contribution of drug-related metabolic alterations to an increased risk for CVD has now emerged as an important concern. As a result of this increased concern, studies have been initiated to reveal the evidence for an the association among these three - HIV infection, its treatment, and CVD. Several studies of adult populations have contributed outstanding results; these studies include retrospective studies such as the Kaiser Permanente Registry study[21], prospective observational cohort studies such as the DAD (Data Collection of Adverse Events of Anti-HIV Drugs) study[22], and prospective randomized clinical trials such as the SMART (Strategies for Management of Antiretroviral Therapy) trial[23]. Initial observations of increased rates of myocardial infarction arising as a result of dyslipidemia in HIV-infected patients on antiretroviral (ARV) drugs[24-26] have been confirmed by studies such as the DAD study, a large, prospective, multi-cohort study that showed associations between ARV therapy and an increased risk of myocardial infarction[22]. Additional well-established CV risk factors such as high smoking rates[27], diabetes and insulin resistance[28], and hypertension[26] are commonly found in HIV-infected persons.

Conventional HAART is composed of a combination of three medications drawn from three main drug classes: nucleoside reverse transcriptase inhibitors (NRTIs, which are nucleoside [or nucleotide] analogues that inhibit the viral reverse transcriptase enzyme[29]), non-nucleoside reverse transcriptase inhibitors (NNRTIs, which also inhibit the reverse transcriptase

enzyme) and protease inhibitors (PIs, which inhibit the activity of the HIV protease)[30]. A HAART protocol generally combines two NRTIs with either a NNRTI or a PI [31]. The decision regarding which dual NRTI combination and which regimen to combine depends on many factors, including CD4+ T cell count, HIV RNA titer, drug interactions, and underlying individual traits such as dyslipidemia. In our study, the immune status of newly-diagnosed HIV infection indicated low CD4+ T lymphocyte counts, supporting the possibility that diagnosis may have been delayed after the primary infection[32]. HIV infection itself is known to cause dyslipidemia[4] due to pro-coagulation and cytokine dysregulation effects associated with HIV infection, HIV interaction with vascular endothelium, and the role of inflammation in AIDS vasculopathy[33-37]. Untreated HIV-infected persons (Naïve status) are more likely to have low levels of cholesterol (total, LDL, and HDL) and elevated serum triglycerides compared to non-HIV-infected persons[38]. In our study, HIV-infected persons at naïve status had lower mean cholesterol concentrations (total, LDL, and HDL) than the non-HIV-infected persons. In contrast to previous studies, no significant differences were observed in serum triglyceride levels between untreated HIV-infected persons (Naïve status) and the non-HIV-infected persons. Our HIV-infected persons at naïve status had lower mean cholesterol concentrations than the non-HIV-infected persons(a healthy control group). This may be an effect of HIV infection itself, which is known to cause dyslipidemia[39]. Decreases in total cholesterol, low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) levels have been reported in men who were infected with HIV[40]. However, in the era of HAART, effective HAART suppresses HIV RNA to undetectable levels, enabling immune recovery, as measured by increases in CD4+ T-cell counts[40]. This is usually accompanied with detectable increases in total cholesterol and LDL-C levels, which some have indicated may be a return to a normal range[39,40]. However, in our study, total

cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels in HAART treated persons were higher than the levels at naïve status.

Several risk scores are used to predict CV risk[41]. The Framingham-based equations have become the most widely used risk scoring system in clinical practice, but a number of other scores have also been introduced, such as the European Systematic Coronary Risk Evaluation (SCORE)[42] algorithm and the Prospective Cardiovascular Munster (PROCAM) model[43], among many others[44-47], have also been reported. The SCORE, derived from European data, enables region-specific and country-specific risk prediction, but it is only applicable to fatal CV events[41]. The other scoring system, PROCAM, is useful when integrating covariates, which may confine clinical adaptation somewhat[41]. The FRS is drawn from data on age, sex, total cholesterol, HDL cholesterol, systolic blood pressure or treatment for hypertension, and presence or absence of cigarette smoking[16]. In addition to traditional risk factors including hypertension, diabetes, dyslipidemia, and cigarette smoking, HIV-associated risk factors possibly influence CVD, perhaps due to peripheral lipoatrophy, reduced adiponectin, increased liver and muscle fat, inflammatory cytokines, low testosterone levels, oxidant stress, hepatitis C virus infection, and PI use[5]. One analysis comparing diabetes risk in persons on antiretroviral therapy with that among matched non-HIV infected persons found impaired glucose tolerance in 35% versus 5% of persons and a greater than 3-fold increased risk of progression to diabetes over 3 years in those receiving antiretroviral therapy[48]. In our study, no significant difference was found in fasting glucose levels (p = 0.1). The currently available evidence from various studies suggests that although the overall CV event rate is low, an added risk of CV events is present in HIV-infected persons compared with non–HIV-infected persons[49,50].

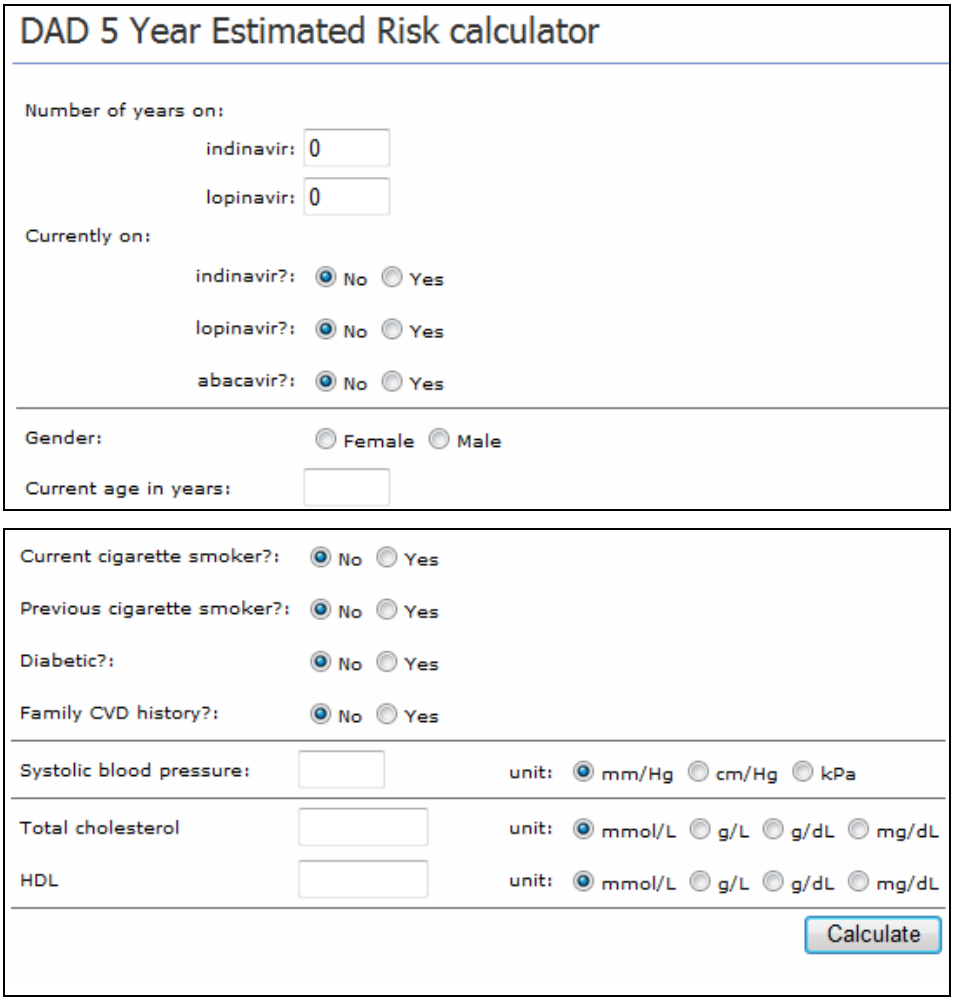
A number of studies have confirmed this CV risk event prediction[13,51]. According to these studies, most HIV-infected persons belonged to the low

risk group regardless of the assessed CV risk prediction tools used[13,51]. In our study, the average 10-year risk for CV events (FRS) was 7.07% (2-45) in the HIV-infected persons and 6.87% (1-37) in the non-HIV-infected persons (p= 0.77) and both belonged to the very low risk group. Among HIV infected persons, the FRS indicated low CV risk in 70.7%, low to moderate risk in 19.9 %, and high risk in 1.7%. In the non-HIV-infected persons, the FRS indicated low CV risk in 80.5%, low to moderate risk in 16.8%, and high risk in 2.7% (p = 0.78). No significant differences were noted between the two groups. This may have arisen from similar smoking rates between both groups and the low body composition of HIV infected persons compared to the non-HIV-infected persons[50,52]. However, one possible concern is that CV risk equations may overestimate or underestimate the absolute risk of CV disease in populations other than the populations used to derive the particular risk equation[53].

Studies on population groups that differ from those used in the derivation of Framingham risk scoring equations have concluded that applying Framingham equations may cause overestimation of the risk of coronary heart disease[52,54-56]. One study demonstrated that the Framingham equation overestimated rates in HIV naïve persons and underestimated rates in treated HIV persons. The authors suggested that features of metabolic syndrome may also increase the risk of myocardial infarction (MI) in HIV treated persons or associations with other drug mechanisms may exist[57]. In the present case, even though most of the HIV-infected persons were assigned to a low risk group, the possibility remains that the actual likelihood of a CV event could be underestimated. In addition, according to the DAD (Data Collection of Adverse Events of Anti-HIV Drugs) study[58], the D:A:D Risk Equations might be more expedient than the conventional risk prediction model for evaluating cardiovascular risks in HIV-infected persons. The D:A:D model evaluates age, sex, systolic blood pressure, smoking status,

family history of CVD, diabetes, total cholesterol, HDL cholesterol, and exposure to indinavir, lopinavir/r and abacavir[58](Fig 2.). It provides a more accurate prediction of the outcomes in the subgroups when compared to the Framingham score. Therefore, the results of our study might be different if D:A:D equation risks are applied.

Fig 2. D:A:D Risk Equations



Evidence suggests that HIV-infected persons on HAART regimens are at increased risk of dyslipidemia, ischemic heart disease[59], and MI, particularly if the HAART regimen contains a PI[60,61]. Previously reports have indicated that HIV-infected persons have decreased total plasma cholesterol before receiving PIs. During PI therapy, an increase in the total and LDL cholesterol levels was also common, whereas HDL levels were heterogeneous[62-64]. Mechanisms by which PIs adversely impact the risk for CVD have also been shown to include impairment of endothelial function and the promotion of atherogenic plaque formation[65-67]. However, the studies on the risk of coronary heart disease among HIV infected persons receiving PI therapy have not shown a consistent association[25,68-71].

These findings prompted the present studies on the association between antiretroviral regimen and metabolic profiles. About 76% of HIV-infected persons in the present study were treated with PI-based HAART and the rest (34%) were treated with NNRTI-based HAART. No significant differences were noted for blood pressure, metabolic profile, FRS, or body composition between the two groups[Table 6.]. At present, several studies have investigated diverse aspects of the relationship between HIV infection, traditional CV risk factors, ART, and short- and longer-term CV risk [21,22,26,59-61,71,72]. These studies have shown that the risk of CVD may increase in HIV-infected versus uninfected populations. However, a few articles have evaluated predictable CV risk by calculating FRS. In our study, no statistical differences were found for the 10-year CV event prediction between HIV infected persons and the non-HIV-infected persons. There was also no difference associated with the type of regimen (NNRTI-based HAART versus PI-based HAART).

V. Conclusion

AIDS mortality due to HIV-related causes has been reduced by HAART. However, non-HIV-related mortality has increased[73]. Reports from recent retrospective and prospective studies performed in large cohorts of HIV-infected persons indicate that a prolonged exposure to combination antiretroviral agents is one of the possible causes for the increased incidence of myocardial infarction. It is therefore necessary to avoid practicing and exploiting HAART just for remarkable benefits it provides. Instead, we must balance the treatment level, taking into consideration the possible impact that it has on the absolute risk of CV events[74].

In our study, contrary to what was expected, approximately 70% of HIV infected persons were categorized into a low CV risk group. In HIV-infected persons on HAART, the 10-year CV risk prediction was similar to that of age- and gender-matched non-HIV-infected persons. However, from the view of combining many factors, even though the results presented here for our study seem to be valid, the possibility remains that actual CV events could be underestimated[57]. With this in mind, the next step for predicting the cardiovascular risk should be calculation of the D:A:D Equation Risks. In addition, the duration of this study was rather short for evaluation of future cardiovascular events, so risk assessment for CVD should be considered for long-term follow-up in HIV-infected persons in their future care.

References

1. Michaels SH, Clark R, Kissinger P. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med 1998;339:405-6.
2. May MT, Sterne JA, Costagliola D, Sabin CA, Phillips AN, Justice AC, et al. HIV treatment response and prognosis in Europe and North America in the first decade of highly active antiretroviral therapy: a collaborative analysis. Lancet 2006;368:451-8.
3. Dube MP, Johnson DL, Currier JS, Leedom JM. Protease inhibitor-associated hyperglycaemia. Lancet 1997;350:713-4.
4. Carr A, Samaras K, Burton S, Law M, Freund J, Chisholm DJ, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. AIDS 1998;12:F51-8.
5. Barbaro G. Highly active antiretroviral therapy-associated metabolic syndrome: pathogenesis and cardiovascular risk. Am J Ther 2006;13:248-60.
6. Krentz HB, Kliewer G, Gill MJ. Changing mortality rates and causes of death for HIV-infected individuals living in Southern Alberta, Canada from 1984 to 2003. HIV Med 2005;6:99-106.
7. Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. Ann Intern Med 2006;145:397-406.
8. Batsis JA, Lopez-Jimenez F. Cardiovascular risk assessment--from individual risk prediction to estimation of global risk and change in risk in the population. BMC Med 2010;8:29.
9. Brindle P, Emberson J, Lampe F, Walker M, Whincup P, Fahey T, et al. Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. BMJ 2003;327:1267.
10. Haq IU, Ramsay LE, Yeo WW, Jackson PR, Wallis EJ. Is the Framingham risk function valid for northern European populations? A comparison of methods for estimating absolute coronary risk in high risk men. Heart 1999;81:40-6.
11. Liu J, Hong Y, D'Agostino RB, Sr., Wu Z, Wang W, Sun J, et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. JAMA 2004;291:2591-9.
12. Marrugat J, D'Agostino R, Sullivan L, Elosua R, Wilson P, Ordovas J, et al. An adaptation of the Framingham coronary heart disease risk function to European Mediterranean areas. J Epidemiol Community

Health 2003;57:634-8.
13. Knobel H, Jerico C, Montero M, Sorli ML, Velat M, Guelar A, et al. Global cardiovascular risk in patients with HIV infection: concordance and differences in estimates according to three risk equations (Framingham, SCORE, and PROCAM). AIDS Patient Care STDS 2007;21:452-7.
14. Law MG, Friis-Moller N, El-Sadr WM, Weber R, Reiss P, D'Arminio Monforte A, et al. The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D Study. HIV Med 2006;7:218-30.
15. Mondy K, Overton ET, Grubb J, Tong S, Seyfried W, Powderly W, et al. Metabolic syndrome in HIV-infected patients from an urban, midwestern US outpatient population. Clin Infect Dis 2007;44:726-34.
16. Hadigan C, Meigs JB, Wilson PW, D'Agostino RB, Davis B, Basgoz N, et al. Prediction of coronary heart disease risk in HIV-infected patients with fat redistribution. Clin Infect Dis 2003;36:909-16.
17. Chung CP, Oeser A, Avalos I, Gebretsadik T, Shintani A, Raggi P, et al. Utility of the Framingham risk score to predict the presence of coronary atherosclerosis in patients with rheumatoid arthritis. Arthritis Res Ther 2006;8:R186.
18. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33 Suppl 1:S62-9.
19. Grunfeld C, Pang M, Doerrler W, Shigenaga JK, Jensen P, Feingold KR. Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Clin Endocrinol Metab 1992;74:1045-52.
20. Kotler DP, Rosenbaum K, Wang J, Pierson RN. Studies of body composition and fat distribution in HIV-infected and control subjects. J Acquir Immune Defic Syndr Hum Retrovirol 1999;20:228-37.
21. Klein D, Hurley LB, Quesenberry CP, Jr., Sidney S. Do protease inhibitors increase the risk for coronary heart disease in patients with HIV-1 infection? J Acquir Immune Defic Syndr 2002;30:471-7.
22. Friis-Moller N, Sabin CA, Weber R, d'Arminio Monforte A, El-Sadr WM, Reiss P, et al. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 2003;349:1993-2003.
23. El-Sadr WM, Lundgren JD, Neaton JD, Gordin F, Abrams D, Arduino RC, et al. CD4+ count-guided interruption of antiretroviral treatment. N Engl J Med 2006;355:2283-96.

24. Passalaris JD, Sepkowitz KA, Glesby MJ. Coronary artery disease and human immunodeficiency virus infection. Clin Infect Dis 2000;31:787-97.
25. Holmberg SD, Moorman AC, Williamson JM, Tong TC, Ward DJ, Wood KC, et al. Protease inhibitors and cardiovascular outcomes in patients with HIV-1. Lancet 2002;360:1747-8.
26. Currier JS, Taylor A, Boyd F, Dezii CM, Kawabata H, Burtcel B, et al. Coronary heart disease in HIV-infected individuals. J Acquir Immune Defic Syndr 2003;33:506-12.
27. Mamary EM, Bahrs D, Martinez S. Cigarette smoking and the desire to quit among individuals living with HIV. AIDS Patient Care STDS 2002;16:39-42.
28. Brown TT, Cole SR, Li X, Kingsley LA, Palella FJ, Riddler SA, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. Arch Intern Med 2005;165:1179-84.
29. Sarafianos SG, Marchand B, Das K, Himmel DM, Parniak MA, Hughes SH, et al. Structure and function of HIV-1 reverse transcriptase: molecular mechanisms of polymerization and inhibition. J Mol Biol 2009;385:693-713.
30. Danner SA, Carr A, Leonard JM, Lehman LM, Gudiol F, Gonzales J, et al. A short-term study of the safety, pharmacokinetics, and efficacy of ritonavir, an inhibitor of HIV-1 protease. European-Australian Collaborative Ritonavir Study Group. N Engl J Med 1995;333:1528-33.
31. Hammer SM, Eron JJ, Jr., Reiss P, Schooley RT, Thompson MA, Walmsley S, et al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. JAMA 2008;300:555-70.
32. Kee MK, Lee JH, Kim GJ, Choi BS, Hong KJ, Lee JS, et al. Decrease of initial CD4+ T-cell counts at the time of diagnosis of HIV infection in Korea; 1988-2006. Int J STD AIDS 2010;21:120-5.
33. Karpatkin S, Nardi M, Green D. Platelet and coagulation defects associated with HIV-1-infection. Thromb Haemost 2002;88:389-401.
34. Bussolino F, Mitola S, Serini G, Barillari G, Ensoli B. Interactions between endothelial cells and HIV-1. Int J Biochem Cell Biol 2001;33:371-90.
35. de Gaetano Donati K, Rabagliati R, Iacoviello L, Cauda R. HIV infection, HAART, and endothelial adhesion molecules: current perspectives. Lancet Infect Dis 2004;4:213-22.
36. Baliga RS, Chaves AA, Jing L, Ayers LW, Bauer JA. AIDS-related

vasculopathy: evidence for oxidative and inflammatory pathways in murine and human AIDS. Am J Physiol Heart Circ Physiol 2005;289:H1373-80.
37. Solages A, Vita JA, Thornton DJ, Murray J, Heeren T, Craven DE, et al. Endothelial function in HIV-infected persons. Clin Infect Dis 2006;42:1325-32.
38. Grunfeld C, Kotler DP, Hamadeh R, Tierney A, Wang J, Pierson RN. Hypertriglyceridemia in the acquired immunodeficiency syndrome. Am J Med 1989;86:27-31.
39. Feeney ER, Mallon PW. HIV and HAART-Associated Dyslipidemia. Open Cardiovasc Med J 2011;5:49-63.
40. Riddler SA, Smit E, Cole SR, Li R, Chmiel JS, Dobs A, et al. Impact of HIV infection and HAART on serum lipids in men. JAMA 2003;289:2978-82.
41. Lloyd-Jones DM. Cardiovascular risk prediction: basic concepts, current status, and future directions. Circulation 2010;121:1768-77.
42. Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987-1003.
43. Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. Circulation 2002;105:310-5.
44. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P. Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. BMJ 2007;335:136.
45. Ridker PM, Paynter NP, Rifai N, Gaziano JM, Cook NR. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. Circulation 2008;118:2243-51, 4p following 51.
46. Ridker PM, Buring JE, Rifai N, Cook NR. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. JAMA 2007;297:611-9.
47. D'Agostino RB, Sr., Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation 2008;117:743-53.
48. Grinspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med

2005;352:48-62.
49. McDonald CL, Kaltman JR. Cardiovascular disease in adult and pediatric HIV/AIDS. J Am Coll Cardiol 2009;54:1185-8.
50. Minguez Gallego C, Vera-Remartinez EJ, Garcia-Guerrero J, Rincon S, Martinez-Rodenas C, Herrero A. [Vascular risk factors in HIV-infected patients in a penitentiary center]. Rev Clin Esp 2011;211:9-16.
51. Cahn P, Leite O, Rosales A, Cabello R, Alvarez CA, Seas C, et al. Metabolic profile and cardiovascular risk factors among Latin American HIV-infected patients receiving HAART. Braz J Infect Dis 2010;14:158-66.
52. Saves M, Chene G, Ducimetiere P, Leport C, Le Moal G, Amouyel P, et al. Risk factors for coronary heart disease in patients treated for human immunodeficiency virus infection compared with the general population. Clin Infect Dis 2003;37:292-8.
53. Thomsen TF, Davidsen M, Ibsen H, Jorgensen T, Jensen G, Borch-Johnsen K. A new method for CHD prediction and prevention based on regional risk scores and randomized clinical trials; PRECARD and the Copenhagen Risk Score. J Cardiovasc Risk 2001;8:291-7.
54. Empana JP, Ducimetiere P, Arveiler D, Ferrieres J, Evans A, Ruidavets JB, et al. Are the Framingham and PROCAM coronary heart disease risk functions applicable to different European populations? The PRIME Study. Eur Heart J 2003;24:1903-11.
55. de Visser CL, Bilo HJ, Thomsen TF, Groenier KH, Meyboom-de Jong B. Prediction of coronary heart disease: a comparison between the Copenhagen risk score and the Framingham risk score applied to a Dutch population. J Intern Med 2003;253:553-62.
56. Thomsen TF, McGee D, Davidsen M, Jorgensen T. A cross-validation of risk-scores for coronary heart disease mortality based on data from the Glostrup Population Studies and Framingham Heart Study. Int J Epidemiol 2002;31:817-22.
57. Koppel K, Bratt G, Schulman S, Bylund H, Sandstrom E. Hypofibrinolytic state in HIV-1-infected patients treated with protease inhibitor-containing highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2002;29:441-9.
58. Friis-Moller N, Thiebaut R, Reiss P, Weber R, Monforte AD, De Wit S, et al. Predicting the risk of cardiovascular disease in HIV-infected patients: the data collection on adverse effects of anti-HIV drugs study. Eur J Cardiovasc Prev Rehabil 2010;17:491-501.
59. Obel N, Thomsen HF, Kronborg G, Larsen CS, Hildebrandt PR,

Sorensen HT, et al. Ischemic heart disease in HIV-infected and HIV-uninfected individuals: a population-based cohort study. Clin Infect Dis 2007;44:1625-31.
60. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab 2007;92:2506-12.
61. Friis-Moller N, Reiss P, Sabin CA, Weber R, Monforte A, El-Sadr W, et al. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med 2007;356:1723-35.
62. Carr A, Samaras K, Thorisdottir A, Kaufmann GR, Chisholm DJ, Cooper DA. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. Lancet 1999;353:2093-9.
63. Periard D, Telenti A, Sudre P, Cheseaux JJ, Halfon P, Reymond MJ, et al. Atherogenic dyslipidemia in HIV-infected individuals treated with protease inhibitors. The Swiss HIV Cohort Study. Circulation 1999;100:700-5.
64. Mulligan K, Grunfeld C, Tai VW, Algren H, Pang M, Chernoff DN, et al. Hyperlipidemia and insulin resistance are induced by protease inhibitors independent of changes in body composition in patients with HIV infection. J Acquir Immune Defic Syndr 2000;23:35-43.
65. Stein JH, Klein MA, Bellehumeur JL, McBride PE, Wiebe DA, Otvos JD, et al. Use of human immunodeficiency virus-1 protease inhibitors is associated with atherogenic lipoprotein changes and endothelial dysfunction. Circulation 2001;104:257-62.
66. Wang X, Chai H, Yao Q, Chen C. Molecular mechanisms of HIV protease inhibitor-induced endothelial dysfunction. J Acquir Immune Defic Syndr 2007;44:493-9.
67. Shankar SS, Dube MP, Gorski JC, Klaunig JE, Steinberg HO. Indinavir impairs endothelial function in healthy HIV-negative men. Am Heart J 2005;150:933.
68. Barbaro G, Di Lorenzo G, Cirelli A, Grisorio B, Lucchini A, Hazra C, et al. An open-label, prospective, observational study of the incidence of coronary artery disease in patients with HIV infection receiving highly active antiretroviral therapy. Clin Ther 2003;25:2405-18.
69. Friis-Moller N, Weber R, Reiss P, Thiebaut R, Kirk O, d'Arminio Monforte A, et al. Cardiovascular disease risk factors in HIV patients--association with antiretroviral therapy. Results from the DAD study. AIDS 2003;17:1179-93.
70. Bozzette SA, Ake CF, Tam HK, Chang SW, Louis TA.

Cardiovascular and cerebrovascular events in patients treated for human immunodeficiency virus infection. N Engl J Med 2003;348:702-10.
71. Mary-Krause M, Cotte L, Simon A, Partisani M, Costagliola D. Increased risk of myocardial infarction with duration of protease inhibitor therapy in HIV-infected men. AIDS 2003;17:2479-86.
72. Bozzette SA, Ake CF, Tam HK, Phippard A, Cohen D, Scharfstein DO, et al. Long-term survival and serious cardiovascular events in HIV-infected patients treated with highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2008;47:338-41.
73. Novoa AM, de Olalla PG, Clos R, Orcau A, Rodriguez-Sanz M, Cayla JA. Increase in the non-HIV-related deaths among AIDS cases in the HAART era. Curr HIV Res 2008;6:77-81.
74. Calza L, Manfredi R, Pocaterra D, Chiodo F. Risk of premature atherosclerosis and ischemic heart disease associated with HIV infection and antiretroviral therapy. J Infect 2008;57:16-32.

< ABSTRACT(IN KOREAN)>

한국에서 HIV 감염인과 정상 건강인의 심혈관 질환에 대한 위험성 비교

<지도교수 김준명>

연세대학교 대학원 의학과

김선빈

배경: 고강도 항레트로바이러스 치료 (HAART)의 도입으로 인해 HIV 감염인들의 생존율이 증가하면서 당뇨, 인슐린 저항성, 이상지혈증, 심혈관계 질환 등 장기 대사 합병증에 대한 관심이 증가하고 있다. Framingham's risk score(FRS)는 연령, 성별, 흡연력, 당뇨력. 혈압, 총콜레스테롤을 포함한 계량화된 값으로 10년 후 심혈관계 질환의 발생 위험도를 예측한다. HIV 감염인과 정상 건강인의 심혈관계 질환에 대한 위험도를 비교한 연구는 거의 시행되어 있지 않다.

방법: 연세대학교 의과대학 세브란스병원에 정기적으로 내원하면서 1년 이상 HAART를 시행 받아 오고 있는 HIV 감염인 116명과 검진 센터에 내원한 정상 건강인 226명을 대상으로 단면 관찰 연구를 시행하였다. HIV 비감염인 중 심혈관 질환으로 치료 중인 환자들은 본 연구에서 제외하였다. HIV 감염인과 정상 건강인 사이의 심혈관계 질환의 위험도를

FRS의 4 범주 (very low risk, low risk, moderate risk, high risk)로 나누어서 양 군간에 위험성에 차이가 있는지 비교 분석하였다.

결과: HIV 감염인과 정상 건강인의 평균 연령은 각각 41세와 40세로 차이가 없었다 (p=0.432). HIV 감염인에서 총 HAART 시행 기간의 중앙값은 38개월이었으며, FRS 평가 당시의 CD4 양성 T 림프구와 혈중 HIV-RNA의 중앙값은 각각 462 개/mm^3, log 1.75 copies/mL이었다. HIV 감염인보다 정상 건강인에서 허리둘레, 체질량 지수가 더 의미 있게 높았다 (82.7 ± 6.9 vs, 86.3 ± 8.3cm, p<0.001; 22.8 ± 2.7 vs, 24.8 ± 3.2kg/m^2,p<0.001) 그러나, HIV 감염인에서 LDL-콜레스테롤이 더 낮고, 중성지방은 더 높았다 (88.9 ± 34.9 vs, 120.5 ± 30.2 mg/dL, p<0.001; 266.2 ± 200.4 vs 151.8 ± 96.3 mg/dL, p<0.001). 이러한 차이에도 불구하고 FRS의 중앙값은 두 군간에 의미 있는 차이를 나타내지 않았다 (7.0 vs, 6.8 점, p=0.768). FRS를 very low risk, low risk, moderate risk, high risk로 구분하여 비교하였을 때에도 두 군간에 의미 있는 차이가 없었다 (p= 0.78)

결론: 높은 빈도의 HIV 감염인 (70%)에서 FRS로 측정한 10년 심혈관계 질환의 위험도가 매우 낮은 것을 확인할 수 있었다. 본 연구 결과를 기반으로 국내 HIV 감염인에서 심혈관계 질환의 유병률이 정상 건강인과 차이가 없는지 장기적인 전향적인 연구가 필요할 것으로 사료된다.

핵심되는 말 : Framingham's risk score; HIV; HIV 감염; HAART; 정상 건강인