Predicted Coronary Heart Disease Risk in Croatian HIV Infected Patients Treated with Combination Antiretroviral Therapy

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A B S T R A C T

We assessed the coronary heart disease (CHD) risk in 130 HIV-infected patients with no major past cardiovascular event treated with combination antiretroviral therapy (CART) between May 2004 and June 2005. We also investigated the association of HIV disease parameters (CD4+ T-cell counts, HIV viral load, AIDS diagnosis, antiretroviral medications and lipodystrophy), demographics, anthropometrics, clinical features, smoking status, dyslipidemia, adherence to the Mediterranean diet, and the metabolic syndrome (MS) to the Framingham risk score. The median 10-year CHD risk was 6.4% (IQR 3.3–13.0) for males and 1.8% (IQR 1.0–6.7) for females. The CHD risk was ≥10% in 31.1% (32 of 103) males and in 14.8% (4 of 27) females. MS was present in 27 (20.8%) individuals. Participants who met the definition of the MS had a 2.63 times greater chance of having a CHD risk ≥10% (95% CI, 1.09–6.39; p=0.032). On multivariable analysis, we found that a CHD risk ≥10% was associated with: a lowest ever CD4+ T-cell counts of less than 50 per microliter and a past history of AIDS (OR, 6.26; 95% CI, 1.61–24.36; p=0.008); alcohol consumption ≥10 g/day (OR, 3.87; 95% CI, 1.56–14.22; p=0.041); and age ≥43 years (OR, 1.30; 95% CI, 1.17–1.45; p<0.001). Interventions to reduce the modifiable cardiovascular risk are needed in Croatian patients treated with CART.

Key words: HIV, coronary heart disease, Framingham risk score, metabolic syndrome

Introduction

Combination antiretroviral therapy (CART) can cause wide spectrum of metabolic abnormalities, dyslipidemia and lipodystrophy (peripheral fat loss and/or visceral obesity)[1,2]. The metabolic changes include hypercholesterolemia, hypertriglyceridemia, insulin resistance, impaired glucose tolerance and type 2 diabetes[2,3]. On the other hand, it has been recognized for almost 25 year that elevated levels of total and low-density lipoprotein (LDL) cholesterol constitute a main risk factor for coronary heart disease (CHD)[4]. The Framingham equation represents a useful tool for calculation the CHD risk, cardiovascular disease or myocardial infarction (MI) risk during the next 5 or 10 years[5]. Assessment of the metabolic syndrome (MS) also provides an accessible diagnostic tool to aid identification of participants with an increased CHD risk[6]. Current guidelines recommended that the risk of cardiovascular disease in HIV-infected patients be estimated from conventional risk-prediction model, such as the Framingham score, which combines different risk factors into numeric estimate of absolute risk[7].

The purposes of the present study were to estimate the prevalence and risk factors associated with the predicted 10 year CHD in participants without an established cardiovascular event. We also examined the association of HIV disease parameters (CD4+ T-cell counts, HIV viral load, and AIDS diagnosis), antiretroviral medications, lipodystrophy, adherence to the Mediterranean diet and the presence of the MS to the Framingham risk score.

Patients and Methods

Study design

We enrolled 130 participants for this analysis, from the study on the effect of the Mediterranean diet on body shape changes and dyslipidemia during CART conducted

on 136 participants from May 2004 to June 2005[8,9]. Participants were under follow-up at the Outpatient HIV/AIDS Department at the University Hospital of Infectious Diseases in Zagreb that provides medical care to the total HIV/AIDS population in Croatia[10]. The study protocol was approved by the institutional review boards of University Hospital of Infectious Diseases in Zagreb.

We included in the study participants older than 18 years, documented HIV-1 seropositive status, had received CART for at least one year, and had lipid measurements. We excluded 6 participants because they already had experienced a cardiovascular event (two of them had myocardial infarction, and four of them had transient cerebral ischemic attack).

Examination protocol

We administered a standard questionnaire to collect demographic data, smoking, and adherence to the antiretroviral treatment. Participants came in the morning having fasted overnight, as recommended in clinical practice. A physical examination and medical history was performed by a physician. Body-shape changes classified in the »lipoatrophy« or »lipohypertrophy« group have been described earlier[8]. Measurements of weight (in kilograms), height (in centimeters) were performed in all participants. Body mass index (BMI) calculated as weight in kilograms divided by the square of height in meters. Participants were defined as normal weight (18.5–24.9), overweight (25.0–29.9) or obese (≥30.0). We dichotomized BMI of our participants into a value zero for participants below 25 and into those equal or above 25. Waist circumference (in cm) was determined using a measuring tape positioned at the point of iliac crest and umbilicus. Blood pressure was measured in the left arm with the elbow flexed to heart level using a mercury sphygmomanometer. Demographic data were collected in a structured interview. Smoking status was classified into two categories, never or past and current. Histories of myocardial infarction, transient cerebral ischemic attack, treatment for hypertension, diabetes type 2, and dyslipidemia were obtained based on interview questions.

Dietary assessment and energy expenditure

The block of 150-item of semi-quantitative food-frequency questionnaire provided by Antonia Trichopolou[11], and translated into Croatian, was used to estimate usual adherence to the Mediterranean diet[8,9]. A scale of 0 to 9 was derived[11], and we dichotomized the Mediterranean diet score into below the median (<4 points, indicating low adherence) and at or above the median (≥4 points, indicating moderate to high adherence to the Mediterranean diet).

The seven-item of International Physical activity Questionnaire translated into Croatian and used to assess energy expenditure[12].

Definition of metabolic syndrome

We used the International Diabetes federation (IDF) definition of the MS[13,14]. Briefly, the MS is present when central obesity defined by a waist circumference >94 cm for Europid men, and >80 cm for Europid women is present, plus any two of following four components: raised triglyceride level ≥1.7 mmol/L, or specific treatment of this lipid abnormality; reduced HDL-cholesterol level <1.0 mmol/L for men and <1.3 mmol/L for women, or specific treatment of this lipid abnormality; raised systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg, or treatment previously diagnosed hypertension; raised fasting plasma glucose ≥5.6 mmol/L, or previously diagnosed type 2 diabetes.

Coronary heart disease risk assessment

We assessed the 10-year CHD risk using algorithm derived from Framingham study[5]. We used Framingham tools from Copenhagen HIV programme[15] that uses algorithms developed and published by Anderson et al.[16]. The variables included in the calculation of 10-year CHD risk are: gender, current age in years, cigarette smoking, diabetes mellitus, left ventricular hypertrophy, systolic blood pressure, total cholesterol and high-density lipoprotein (HDL)-cholesterol. Predicted risk of CHD was classified as moderate to high when it was at ≥10% in the next 10-years.

Biologic measures

We directly measured fasting plasma glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides by standard enzymatic techniques on *Olympus AU400*. Viral load was obtained by polymerase chain reaction, using the Amplicor Monitor RT-PCR assay (Roche Molecular Systems) with lower limit detection of 50 or 400 copies/mL. We performed CD4 lymphocyte counts by flow cytometry.

Antiretroviral treatments

We recorded three categories of antiretroviral drug combinations (CART): currently receiving a non-nucleoside reverse-transcriptase inhibitor (NNRTI) based CART, a protease inhibitor (PI) combination or using both. We also recorded the use of each antiretroviral drug, and duration of administration.

Statistical analysis

We expressed our data with frequencies for categorical variables, median, and interquartile ranges for quantitative variables. The calculated 10-year CHD risk was dichotomized at ≥10% and used in bivariable and multivariable analysis. We used the Wilcoxon-Mann-Whitney test for comparisons of non-normally distributed quantitative variables. For comparison of the categorical variables we used Fisher exact tests, χ^2-tests or odds ratios (OR) with 95% confidence intervals (CI). We included into the multivariable logistic regression analysis HIV disease factors significantly associated with a moderate-to high CVD risk (nadir CD4 cell count, history of AIDS, viral load). Also included were other variables found significant in bivariable analysis. Except for age other components of the Framingham equation (sex,

Characteristics*	10-year risk of coronary heart diseases ≥10%				p value
	10-y-CHD <10% n=94 (72%)		10-y-CHD ≥10% n=36 (28%)		
Age, years	39	(34–45)	54	(49–60)	<0.001
Body mass index, kg/m^2	23.5	(21.3–26)	25.6	(24–27.6)	0.005
Waist circumference, cm	87	(81–92)	90	(85.5–97.5)	0.003
Hip circumference, cm	91	(86–95)	94	(90–99.5)	0.008
Systolic blood pressure, mm Hg	120	(110–130)	130	(120–145)	<0.001
Diastolic blood pressure, mm Hg	75	(70–80)	90	(80–90)	<0.001
Total cholesterol, mmol/L	5.3	(4.6–6.0)	6.4	(5.7–7.0)	<0.001
HDL-cholesterol, mmol/L	1.2	(1.0–1.5)	1.1	(1.0–1.3)	0.173
LDL-cholesterol, mmol/L	3.5	(3.0–3.9)	4.0	(3.4–4.6)	0.013
Trigliceridi, mmol/L	2.1	(1.4–3.0)	2.3	(1.8–4.9)	0.025
Glucose, mmol/L	4.8	(4.4–5.3)	5.3	(4.8–5.8)	0.002
Log plasma HIV RNA	5.5	(5.0–5.8)	5.8	(5.4–6.0)	0.030
Duration of HIV infection, years	5.3	(2.2–8.3)	6.1	(4.1–8.3)	0.375
Duration of treatment, years	3.0	(2.0–5.0)	5.0	(2.5–6.0	0.004

*Values are medians and interquartile ranges

smoking, hypertension, cholesterol and HDL) were not included into the multivariable analysis. In this analysis, we dichotomized the age of our participants at the median (43 years). The final model included HIV disease variables and other non-HIV disease variables which suggested an association with the outcome. The analyses were done using SAS version 9.1.3 software (SAS institute INC, Cary, North Carolina, USA) and the level of significance was at the 0.05 level.

Results

Participant characteristics

The median age of 130 participants was 43.0 (IQR, 36–49) years. The median 10-year Framingham predicted CHD score was 5.6% (IQR, 2.5–11.0). It was 6.4% (IQR, 3.3–13.0) for males and 1.8% (IQR, 1.0–6.7) for females. Thirty-six (28%) participants had a 10-year CHD risk of ≥10%, and 5 (4%) participants had 10-year CHD risk higher than 25%.

Forty-three percent acquired HIV through heterosexual sex, 40% through sex between men and 10% through injecting drugs 2% from blood products and in 5% the route of infection was unknown.

Sixty-five (50%) of participants were current smokers. Moderate alcohol consumption (10 to 30 g/day) was reported by 31 (24%) and heavy alcohol consumption (≥30 g/day) was reported by 18 (14%).

Metabolic syndrome

Among 130 HIV infected participants (males: 103, 79%), there were 27 (21%) participants who reached the condition-specific cut points for MS. MS was found more frequently in females (10/27, 37%) then in males (17/103, 17%; p=0.031). We found that 78 (60%) of HIV-infected participants had a normal body mass index (BMI: <25), 42 (32%) were overweight (BMI: ≥25), and 10 (8%) were obese (BMI: ≥30). The prevalence of high blood pressure >130 mmHg) was 56 (43%) and >140 mm Hg in 13 (10%) of participants. Abdominal obesity was found in 42 (32%) participants. Females were more frequently to have abdominal obesity (14/27, 52%) than males (28/103, 27%; p=0.021). The prevalence of elevated blood glucose >6 mmol/L was 12 (9%).

Non-HIV-related factors associated with CHD risk.

We dichotomized the 10-year CHD risk at ≥10% and selected clinical features and laboratory measurements are presented in Table 1 and 2. Abdominal obesity defined by waist circumference measurements and by hip circumference measurements were weakly correlated to the 10-year CHD risk (r=0.34; p<.001 and r=0.25; p=0.004, respectively). In bivariable analysis, a significant difference between participants with a high 10-year CHD risk at ≥10% compared with those with low 10-year CHD risk at <10% was observed for BMI ≥25.0 (OR 3.35; 95% CI, 0.41–8.82; p=0.003), hypertension (systolic blood pressure ≥140 mm Hg, and or diastolic blood pressure ≥90 mm Hg; OR 8.98; 95% CI, 3.73–21.61; p<0.001), total cholesterol >5.0 mmol/L (OR 5.23; 95% CI, 1.87–14.61; p=0.002), ethanol drinking ≥10 g/days (OR 2.77; 95% CI, 1.26–6.13; p=0.012). Participants who met the definition of the MS had a 2.63 times greater chance of having a CHD risk ≥10% (95% CI, 1.09–6.39; p=0.032).

TABLE 2
COMPARISON OF 10-YEAR CORONARY HEART DISEASE RISK AND DIFFERENT CHARACTERISTICS OF 130 HIV INFECTED
PARTICIPANTS (CATEGORICAL VARIABLES)

| Characteristics | 10-year risk coronary heart disease ≥10% | | | | | OR | 95% CI | p |
| | 10-y-CHD <10% | | 10-y-CHD ≥10% | | | | | |
	n=94 (72%)		n=36 (28%)					
Male gender (yes versus no)	71	76%	32	89%		0.39	0.12–1.21	0.102
Hypertension* (yes versus no)	14	15%	22	61%		8.98	3.73–21.61	<0.001
Body mass index ≥25 (yes versus no)	30	32%	22	61%		3.35	1.51–7.45	0.003
Alcohol consumption ≥10 g/day (yes versus no)	19	53%	27	29%		2.77	1.26–6.13	0.012
Metabolic syndrome (yes versus no)	15	16%	12	33%		2.63	1.09–6.39	0.032
CD4 <50 per μL (yes versus no)	33	35%	22	61%		2.91	1.32–6.42	0.008
AIDS diagnosis (yes versus no)	36	38%	23	64%		2.85	1.28–6.33	0.01
Viral load peak >300 000 copies/mL(yes versus no)	46	49%	26	72%		2.71	1.18–6.25	0.019
Lipoatrophy (yes versus no)	35	37%	17	47%		1.51	0.69–3.28	0.3
Lipohypertrophy (yes versus no)	26	28%	16	44%		2.09	0.94–4.65	0.07
Lipodystrpophy (yes versus no)	47	50%	23	64%		1.77	0.80–3.90	0.158
Pretreated with								
Protease inhibitors (yes versus no)	66	70%	30	83%		2.12	0.80–5.66	0.133
Non-nucleoside analogues (yes versus no)	60	64%	28	78%		1.98	0.81–4.84	0.132
Currently treated with								
Protease inhibitors (yes versus no)	43	46%	15	42%		0.85	0.39–1.84	0.676
Non-nucleoside analogues (yes versus no)	49	52%	23	64%		1.63	0.74–3.59	0.229

*Hypertension was defined as raised systolic blood pressure ≥140 mm Hg and or diastolic blood pressure ≥90 mm Hg, or treatment of previously diagnosed hypertension

An overall estimate for blood pressure ≥130 mm Hg was 43 (42%) in men and 13 (48%) in women, for total cholesterol greater than 5 mmol/L was 63 (61%) in men and 19 (70%) in women, and for BMI ≥25 was 42 (41%) in men and 10 (37%) in women. Adherence to the Mediterranean diet, energy expenditure ≥8.6 MET-h/days, consumption of olive oil, current smoking, and family history of CHD were not associated with the dichotomized CHD risk score.

HIV-related factors associated with CHD

Using bivariable analysis (Table 2), we identified HIV-related factors associated with 10-year CHD risk ≥10%: history of AIDS diagnosis (OR 2.85; 95% CI, 1.28–6.33; p=0.010); higher viral load (OR 2.71; 95% CI, 1.18–6.25; p=0.019) and CD4 count <50 *per* mm³ (OR 2.91; 95% CI, 1.32–6.42; p=0.008).

A lower mean HDL-cholesterol we found in participants who had a CD4 count ≤50 (mean 1.2±0.4 mmol/L *vs.* mean 1.3±0.3 mmol/L; p=0.047). A higher mean total cholesterol was found in participants who had lipohypertrophy (mean 6.0±1.2 mmol/L *vs.* mean 5.5±1.2 mmol/L; p=0.020).

Combination antiretroviral treatment

Fifty-eight participants (45%) used currently a PI, and 72 (55%) used currently NNRTI CART. There was no association with the type of CART and a higher risk

10-year CHD. Higher mean total cholesterol was found in participants treated with PI-based compared to non-PI-based CART (mean 5.8±1.2 mmol/L *vs.* mean 5.2±1.2 mmol/L; p=0.031). In participants, who had received nevirapine we observed a higher 10-year CHD risk at ≥10% (OR 2.90; 95% CI, 1.11–7.60; p=0.030) compared to non-nevirapine regimens, while exposure to the other antiretroviral medications was not associated with a higher 10-year CHD risk at ≥10%.

Multivariable analysis

In multivariable analysis (Table 3), participants who had an age ≥43 years, a CD4 count less than 50 *per* microliter plus history of AIDS diagnosis, as well as alcohol consumption ≥10 g/day were more likely to have a 10-year CHD risk ≥10%. Overweight or obese participants increased the likelihood of CDH risk, but the difference was not significant.

Discussion

We found that more than one quarter of our participants had a 10-year CHD risk of ≥10%. This finding corresponds with a previous Italian report in which a 10-year CHD risk of ≥10% was found in 22% of HIV infected participants, and a 10-year CHD risk above 20% was found in 6% of participants[17]. In our study, the median CHD

risk was 6.4% (mean age 44 years) for man and 1.8 (mean age 41.4 years) for woman. This is similar or less compared to findings from Germany, Norway or USA. In a German cohort the median of 10-year CHD risk was estimated to be 9% in HIV infected men (mean age, 43 years) and 2% in HIV infected women (mean age 37 years)[18]. In a cohort from Oslo the mean 10-year CHD risk was 9% (about 80% men, mean age 41 years)[19], and in a large American multicentre study the median CHD risk was 6% (mean age 46 years) in HIV infected man and 2% (mean age 42 years) in HIV infected woman[20]. In the study by De Socio et al.[17] the average 10-year CHD risk was 7% in HIV infected participants. In addition, the estimated CHD risk was higher in HIV infected participants treated with CART compared to age matched group of HIV uninfected participants of the general population[17,21].

We identified a number of factors related to the 10-year CHD risk of ≥10%: older age, higher BMI, waist circumference, hip circumference, hypertension and total cholesterol. These findings are expected and consistent with prior evidence that conventional risk factors such as smoking, hypertension, total cholesterol, decreased HDL-cholesterol, increased triglycerides, diabetes and family history were all significantly associated with MI in HIV-infected participants[22].

Based on the calculation of BMI we estimated that 32% of HIV-infected participants were overweight, and 8% of them were obese. Jacobson et al reported that 35% of HIV infected participants were overweight and 18% were obese in the USA[23]. Of note, we found that 41% of HIV-infected men and 37% of woman were overweight or obese based on a BMI ≥25. This is in agreement with recent study for men, but we found twice less women met criteria for being overweight. We found that participants with higher BMI have a three times higher 10-year CHD risks of ≥10% (Table 2).

Our results suggest that the total cholesterol is a stronger predictor of CHD risk than LDL-cholesterol. Others found that total cholesterol and LDL-cholesterol are similar in their ability to predict initial CHD events[5]. Higher waist circumference was associated with a greater 10-year CHD risk. Waist circumference is not primarily driven by the inclusion of 10-year CHD risk in the definition.

Our results showed that alcohol consumption is associated with a higher 10-year CHD risk. This is in contrast with a recent study in which participants who had ≥14 drinks per week compared by abstainers had significantly decreased predicted CHD[20]. However, this has been explained by selection bias; individuals at highest cardiac risk were more likely to receive physician advice to curtail their alcohol consumption, or early death of heavy drinkers at highest CHD risk[20]. We found that 50% of participants were current smokers which contributed significantly to a higher CHD risk.

The prevalence of MS was 21% in Croatian HIV-infected participants which is similar to 27% found in Danish HIV-infected patients[24]. A recent French study found a lower prevalence of MS (7.4%) in HIV infected men[25], and 5.9% in HIV uninfected French men[26]. A study from the UK found the prevalence of MS of 10%[27]. The prevalence of MS was 24% in HIV positive participants in the greater Boston area or Rhode Island[23]. The estimated prevalence of MS was 17% in HIV-infected participants from Barcelona and increased to 27% for those aged 50–59 years[28]. In a large international study the prevalence of MS in HIV-infected participants was 14–18%[29]. In an Italian study MS was in 22% of HIV infected participants[30]. In addition the prevalence of MS was higher in HIV infected participants treated with CART compared to group of HIV uninfected participants of the general population[31]. The MS was highly predictive for development of diabetes[29,32], as well as increased risk of cardiovascular events[6,33]. We found that female participants were somewhat more likely to have MS, but the statistical difference was not significant.

A consistent finding in our analysis was a strong association between lower CD4 T-cell counts and higher 10-year CHD risk. Others have also reported that a lower CD4 T-lymphocyte count is associated with a higher cardiovascular risk[34,30]. The duration and severity of immunosuppresion in HIV infected individuals might be a risk factor for ischemic cardiovascular diseases[34]. In addition Escaut et al. observed that MI was associated with a lower mean CD4 T-cell count in HIV-infected individuals compared with those without MI[35]. Lower CD4 T-lymphocyte counts might also be risk factor, even the marker for MI[34]. AIDS diagnosis was associated with a higher CHD and this is also consistent with findings from a US multicentric analysis[20]. It may reflect adverse metabolic changes among those with advanced disease[36]. However, using multivariable analysis in our study only partici-

TABLE 3.
MULTIVARIABLE ANALYSIS OF FACTORS RELATED TO MODERATE TO HIGH CORONARY HEART DISEASE RISK AMONG 130 HIV INFECTED PATIENTS

Variable	OR	95% CI	p
Age ≥43 years	1.30	1.17–1.45	<0.001
Alcohol consumption ≥10 g/day	3.87	1.56–14.22	0.041
BMI overweight or obese	3.01	0.88–10.27	0.079
CD4 <50 per μL and AIDS diagnosis	6.26	1.61–24.36	0.008
Viral load peak >300 000 copies/mL	1.30	0.36–4.77	0.691

* Moderate CHD risk was defined as 10-year risk ≥10%

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pants with both an AIDS history and with a nadir CD4 cell of less than 50 per microliter had a 10-year CHD risk ≥10%. We did not find an association between the 10-year CHD risks and PI-based or NNRTI-based treatment.

This study has several limitations. The sample size is relatively small, and the design of this study was cross-sectional, so generalizations of these finding should be made with caution. Biases are inherent in observational studies, for example the association of nevirapine use and 10-year CHD ≥10% was observed in our study because nevirapine has a favorable lipid profile and thus we used it when the CHD risk was high. Nevertheless the main finding that a low nadir CD4 cells count and a history of AIDS is associated with a higher CHD risk is in concordance with findings from larger studies.

In conclusion, as survival of HIV infected participants increases[37] cardiovascular complications are becoming more important. We found that a significant number of HIV infected participants have a moderate to high CHD risk which needs to be addressed in routine care. Advanced HIV disease can also be associated with a higher CHD risk, hence earlier treatment and diagnosis of HIV-infection is important. In Croatia up to 35% of participants presented to care with AIDS in recent years[38]. Although the Mediterranean diet is associated with longevity we did not find an association between adherence to the diet and lower CHD risk calculated by the Framingham equation.

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PREDVIĐANJE RIZIKA KORONARNE BOLESTI SRCA U SUDIONIKA ZARAŽENIH HIV-OM IZ HRVATSKE LIJEČENIH CART-OM

S A Ž E T A K

Procijenili smo rizik koronarne bolesti (KB) u 130 sudionika zaraženih HIV-om, liječenih kombinacijom antiretrovirusnih lijekova (CART) koji nisu ranije imali veća kardiovaskularna oštećenja od svibnja 2004 do lipnja 2005. Također smo istražili povezanosti parametara HIV bolesti (broj CD4+ T stanica, stupanj HIV-viremije, AIDS dijagnoza, antiretrovirusni lijekovi, lipodistrofija) demografske, antropometrijske, kliničke odlike, pušački status, dislipidemiju, pridržavanje mediteranskoj prehrani i metabolički sindrom (MS) u odnosu na računanje Framingham-ovog rizika. Medijan desetgodišnjeg rizika KB je 6,4% (IQR 3,3–13,0) za muške i 1,8% (IQR 1,0–6,7) za ženske. Rizik od KB ≥10% je 31,1% (32 od 103) u muških i 14,8% (4 od 27) u ženskih. MS je bio prisutan u 27 (20,8%) pojedinaca. Sudionici sa MS imali su 2,63 puta veću šansu imati rizik KB ≥10% (95% CI 1,09–6,39; p=0,032). U multivarijatnoj analizi našli smo da će ispitanici imati rizik KB ≥10%: ako su ikad imali broj CD4+ T-stanica manje od 50 po mikrolitru i AIDS definirajuću bolest u anamnezi (OR 6,26; 95% CI 1,61–24,36; p=0.008); konzumirali alkohol ≥10 g/dnevno (OR, 3,87; 95% CI 1,56–14,22; p=0,041); i bili u dobi ≥43 godine (OR, 1,30; 95% CI 1,17–1,45; p<0,001). Potrebne su intervencije koje smanjuju promjenjive kardiovaskularne rizike u hrvatskih bolesnika koji se liječe CART-om.