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Cardiovascular Disease Prevention Counseling Program for Systemic Lupus Erythematosus Patients

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Abstract

Objective—To determine if a cardiovascular disease prevention (CVD) counseling program for lupus patients decreases the prevalence of CVD risk factors.

Methods—The *assessment* phase of three-year CVD prevention counseling program included the evaluation of CVD risk factors, diet, exercise habits, and medications. The *education* phase included discussion of the above risk factors as well as CVD and thrombosis prevention strategies. Patients were prospectively followed every 3–6 months for risk assessment and continued education by a nurse practitioner and a medical doctor.

Results—Between March 2009 and December 2014, 121 patients were included. At baseline, abnormal blood pressure, blood glucose, cholesterol profile, and body mass index were found in 50 (41%), 7 (6%), 82 (68%), and 77 (64%) of patients, respectively. During the three-year follow-up, among those with abnormal baseline values: a) prevalence of abnormal blood pressure significantly decreased (OR: 0.94, 95% CI: 0.92–0.96, $p < 0.0001$) with significant mean systolic blood pressure improvement (-6.12 ± 2.16 mmHg, $p < 0.05$); b) prevalence of abnormal cholesterol profile significantly decreased (OR: 0.90; 95% CI: 0.92–0.96) with significant improvements in mean high-density lipoprotein ($+5.4 \pm 0.36$ mg/dl, $p < 0.0001$) and mean triglyceride levels (-12.6 ± 0.81 mg/dl, $p < 0.05$); and c) no significant change in blood glucose and body mass index were observed. At baseline, 100 (83%) and 95 (79%) patients had poor diet and physical activity; during the follow-up, both significantly improved in the entire population.

Conclusion—Our data suggest that a CVD prevention counseling program decreases the prevalence of some CVD risk factors in lupus patients.

Keywords

lupus; cardiovascular disease; prevention; counseling

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INTRODUCTION

Although the prognosis of systemic lupus erythematosus (SLE) has dramatically improved with a 50% decreased mortality rate since the early 2000's (1), cardiovascular disease (CVD) remains a major cause of mortality in SLE patients (2–6). Premature CVD is more common in young premenopausal women with SLE than in age- and sex-matched controls; women with SLE are five times more likely to have acute myocardial infarction, and an fifty times more likely to have atherosclerosis-related events compared to age and gender matched-controls (7).

Increased risk of CVD in SLE is only partially explained by conventional CVD risk factors; SLE-related factors also contribute to the risk (7). Some of these factors are modifiable, e.g., lupus activity, hypertension, dyslipidemia, obesity, and sedentary lifestyle, whereas others are non-modifiable, e.g., disease duration, steroid dose and duration, chronic renal disease, gender, older age, post-menopausal status, family history, and antiphospholipid antibodies (aPL) (8).

Given the importance of well-controlled disease activity and traditional CVD risk factors in the management of lupus patients, we developed a free-of-charge CVD Prevention Counseling Program for SLE patients that provided a basic assessment of and education about CVD risk factors. The objective of this study (“program evaluation”) was to assess the effectiveness of the CVD- Prevention Counseling Program in decreasing the prevalence of CVD risk factors in SLE patients.

PATIENTS AND METHODS

Study Population

Systemic Lupus Erythematosus patients followed at our tertiary care institution, during their follow-up visits, were invited by their physicians to participate in a free-of-charge three-year CVD- Prevention Counseling Program. Initial referral was based on physicians' clinical diagnosis of “SLE”; however, patients fulfilling three or more American College of Rheumatology SLE Classification Criteria were allowed to participate in CVD- Prevention Counseling Program.

The Cardiovascular Disease Prevention Counseling Program

The CVD- Prevention Counseling Program program baseline visit consisted of two phases. The *assessment* phase included the evaluation of blood pressure, blood glucose, cholesterol profile, body mass index (BMI), smoking, life style habits (diet and exercise), aPL-profile, and medications. The *education* phase for patients, independent of the CVD risk level, included detailed discussion of the above risk factors as well as CVD and thrombosis prevention strategies. At the end of each visit patients: a) received tailored lifestyle recommendations and a written summary report; and b) were referred to a registered dietitian as needed based on pre-set criteria. Current smokers were referred to New York Presbyterian Hospital Smoking Cessation Program and to New York City Quit Smoking telephone line. At the baseline visit, patients also completed an anonymous survey about

their CVD risk awareness and general diet/exercise habits. In addition, patients' physicians received a summary report.

During the three-year follow-up, patients were followed every 3–6 months (based on their baseline risk) for CVD risk factor re-assessment and for continued education by trained personnel (a nurse practitioner and a medical doctor) in a standardized format. Patients also received regular newsletters, pamphlets, and brochures about CVD risk factors and prevention strategies. At each follow-up visit, questions about diet/exercise habits were repeated.

Cardiovascular Disease Risk Assessment

During each CVD- Prevention Counseling Program visit, following the assessment of different CVD risk factors, “abnormal” values were defined as: a) systolic blood pressure > 120 mmHg; b) diastolic blood pressure > 80 mmHg; c) random blood glucose > 130 mg/dl or fasting blood glucose > 100 mg/dl for non-diabetic patients; d) pre-prandial and post-prandial blood glucose > 130 mg/dl and 180 mg/dl, respectively for diabetic patients; e) hemoglobin A1c (HBA1c) levels > 7% and > 5.7% for diabetic and non-diabetic patients, respectively; and f) total cholesterol > 200 mg/dl, total low-density lipoprotein (LDL) levels > 130 mg/dl (100 mg/dl for high CVD risk patients), high-density lipoprotein (HDL) < 50 mg/dl for women (40 mg/dl for men), or triglycerides (TG) 150 mg/dl; and g) BMI 25 kg/m². “Poor diet” was defined based on at least three of the following: a) limited fruits and vegetables on a weekly basis; b) limited whole-grain, high fiber foods on a weekly basis; c) fish less than twice a week; d) alcohol intake more than one drink/day (12 oz. beer or 5 oz. glass of wine); and e) high-cholesterol diet (defined based on the assessments of total, saturated, and trans fat intake, amount of dietary cholesterol and total fat in total calories, and amount of egg yolks per week). “Poor physical activity” was defined as less than 30 minutes of moderate-intensity aerobic activity daily.

Metabolic syndrome was defined following the National Heart, Lung, and Blood Institute/American Heart Association definition, as a combination of at least two of the following: a) abdominal circumference > 88 cm for women (> 102 cm for men); b) TG 150 mg/dl; c) HDL < 50 mg/dl for women (40 mg/dl for men); d) blood pressure 130/85 mmHg; e) fasting glucose 110mg/dl (Scott Circulation 2004). Positive aPL was defined as positive lupus anticoagulant [LA] test, anticardiolipin antibody [aCL] enzyme-linked immunosorbent assay [ELISA] IgG/M 40U, and/or anti-β2-Glycoprotein-I antibody IgG/M 40U at least twice 12 weeks apart. Antiphospholipid Syndrome was defined based on the Updated Sapporo APS Classification Criteria (9).

Patients with BMI 25 and/or a poor diet were referred for nutritional counseling, which included recommendations set by Therapeutic Lifestyle Changes for cholesterol reduction and patient-centered methods for dietary behavior change as detailed in our subgroup analysis (10).

Statistical Analysis

Data were summarized using descriptive statistics. Patients without three-year follow-up were censored at their last follow-up. Sub-group comparisons were made by using T-test or

Wilcoxon rank sum test for continuous variables, and Chi-Square or Fisher's exact test for categorical variables. While analyzing the three-year outcomes, linear and generalized mixed effect models were used (includes all the measurements from baseline to the last visit) to evaluate whether CVD risk factors improved over time after controlling for age, gender, race, BMI, and baseline blood glucose, cholesterol profile, diet habits, and physical activity level. Data were assumed to be missing at random and the above likelihood-based models yielded valid inferences based on this assumption. All statistical tests were two-tailed with a significance level of 0.05. All analyses were performed using SAS 9.3 (SAS Institute, Inc. Cary, NC).

The CVD- Prevention Counseling Program was partially supported by the New York Community Trust, New York, NY. The retrospective analysis of the prospectively collected data was approved by the Institutional Review Board of our institution.

RESULTS

Baseline Characteristics

Between March 2009 and December 2014, 121 patients completed 696 visits (mean: 4.7 ± 3.7 ; range: 1–13). The mean and median follow-ups were 22.8 ± 14.5 and 36 months, respectively. Demographic and baseline clinical characteristics of the study population are shown in Table 1. Seventy-seven (64%) patients were overweight or obese with a mean BMI of 28.4 (16.5–49.9). Based on 107/121 (88%) who completed the baseline CVD awareness survey, 42% of participants reported that they were not aware of their CVD risk, 36% had some but limited knowledge, and 22% were aware of their CVD risk.

Three-year Completion Rate

Sixty-two (51%) patients completed the three-year follow-up. Among those who did not complete the three-year follow-up, 24 (20%) patients were lost-to-follow-up for unknown reason, 21 (17%) patients transferred their care to another institution or moved out of state, 11 (9%) patients were not interested in the program after a number of visits, and three (2%) patients died. Deaths were due to congestive heart failure secondary to end-stage renal disease, hip fracture-related complications, and stroke. Patients who did not complete the three-year follow-up were less likely to be African-American and more likely to have history of hypertension (Table 1).

Blood Pressure Assessment During the Follow-up

The mean baseline systolic and diastolic blood pressure were 118 ± 15.9 mmHg and 73 ± 9.9 mmHg, respectively. During the 3-year follow-up, there were no significant changes in the percentage of patients with abnormal blood pressure, mean systolic blood pressure, and mean diastolic blood pressure (Table 2). In a subgroup analysis of 50 (41%) patients with abnormal baseline systolic and/or diastolic blood pressure (mean 133 ± 12 mmHg and 81 ± 9 mmHg, respectively), there was a significant decrease in: a) the number of patients with abnormal blood pressure (Odds Ratio [OR]: 0.94, 95% Confidence Interval [CI]: 0.92–0.96); and b) in mean systolic blood pressure (-6.12 ± 2.16 mmHg) over time in the multivariate

analysis. Furthermore, the majority of life style habits (diet and physical activity) significantly improved in this subgroup (Table 3).

Blood Glucose Assessment During the Follow-up

The mean baseline blood glucose was 88 ± 34 mg/dl. During the 3-year follow-up, there was no significant change in mean blood glucose; moreover, the percentage of patients with abnormal blood glucose significantly increased over time (OR: 1.11, 95% CI: 1.08–1.15) (Table 2). In a subgroup analysis of 7 (6%) patients with abnormal baseline blood glucose (mean 150 ± 122 mg/dl), there was a significant decrease in mean blood glucose (-42.12 ± 18 mg/dl) and BMI over time in the multivariate analysis, but not in the number of patients with abnormal blood glucose (Table 3).

Cholesterol Profile Assessment During the Follow-up

The mean baseline cholesterol profile was: total cholesterol 178 ± 34 mg/dl, LDL 100 ± 30 mg/dl, HDL 55 ± 18 mg/dl, and TG 118 ± 61 mg/dl. During the 3-year follow-up, only mean HDL significantly improved (Table 2). In a subgroup analysis of 94 (78%) patients with baseline abnormal cholesterol profiles (mean total cholesterol 183 ± 36 mg/dl, LDL 107 ± 30 mg/dl, HDL 51 ± 20 mg/dl, and TG 129 ± 68 mg/dl), there was a significant improvement in the number of patients with abnormal cholesterol profile (OR: 0.90, 95% CI: 0.92–0.96), mean HDL ($+5.4 \pm 0.36$ mg/dl), and mean TG (-12.6 ± 5.4 mg/dl) in the multivariate analysis. Furthermore, the majority of life style habits (diet and physical activity) significantly improved in this subgroup (Table 3).

Body Mass Index Assessment During the Follow-up

The baseline BMI was 28.4 ± 7 kg/m². During the 3-year follow-up, there was no significant change in BMI. In a subgroup analysis of 76 (64%) patients with abnormal baseline BMI (mean 32 ± 6 kg/m²), no significant change was observed in mean BMI or in the number of patients with abnormal BMI in the multivariate analysis (Table 3). However, the majority of life style habits (diet and physical activity) significantly improved in this subgroup (Table 3).

Smoking Assessment During the Follow-up

During the 3-year follow-up, when all patients were analyzed as a group, no significant change in percentage of “current smokers” was found. Among the eight (7%) patients who were active smokers at baseline: a) only 2/8 (25%) were seen at the New York Presbyterian Smoking Cessation Program for the initial consultation with no regular follow-ups; and b) all were still smokers at the time of their last visits (three completed the three-year follow-up and four did not).

Diet Assessment During the Follow-up

During the 3-year follow-up, for all patients, the percentage of patients categorized as having “poor diet” significantly decreased, while those who consumed a diet rich in fruits and vegetables, whole-grain and high fiber, fish at least twice a week, alcohol intake not more than one drink/day, and cholesterol free products significantly increased (Table 2). In a subgroup analysis of 100 (83%) patients with baseline “poor diet”, the number of patients

with poor diet habits significantly decreased over time (OR: 0.93, 95%CI: 0.91–0.95). Those patients also significantly increased their intakes of rich fruit and vegetables (OR: 1.06, 95%CI: 1.04–1.08), grain and fiber diet (OR: 1.07, 95%CI: 1.05–1.09), fish twice a week (OR: 1.04, 95%CI: 1.02–1.06), and cholesterol free diet (OR 1.03 95%CI: 1.01–1.05) (Table 3). Furthermore, the physical activity (30 mins/day) of this subgroup significantly improved.

Physical Activity Assessment During the Follow-up

During the 3-year follow-up, the percentage of patients who had poor physical activity significantly decreased, and the percentage of patients who exercised 30 mins/day moderate physical activity significantly increased, but no significant change in the percentage of patients who performed 60–90 mins/day moderate physical activity, in whom the goal was to lose or sustain weight, was observed (Table 2). However, for the 95 (79%) patients with poor physical activity at baseline, the number of patients with poor physical activity significantly decreased (OR 0.93, 95%CI 0.92–0.96), and the number of patients who exercise 30 mins/day significantly increased (OR: 1.05, 95%CI: 1.03–1.07). Furthermore, the majority of the diet habits of this subgroup significantly improved (Table 3).

Subgroup Assessment of Patients Based on Corticosteroid Use

When we compared 82 (68%) patients who ever used corticosteroids during the counseling period to those who never used corticosteroids, there was no significant difference between two groups, except for changes in cholesterol profile and physical activity over time. Patients who ever received corticosteroids were less likely to decrease their mean total cholesterol and LDL levels, and less likely to improve their physical activity compared to those who never received corticosteroids (OR: 0.5, 95% CI: 0.25–0.99). Holding other factors constant, the total cholesterol of patients who received corticosteroids was 15 ± 6 mg/dl higher, and the LDL level 14 ± 5 mg/dl higher, than those who did not receive corticosteroids over time.

Discussion

Our program evaluation, investigating the effect of a free-of-charge CVD prevention counseling program on the prevalence of CVD risk factors in SLE patients, demonstrate that patients with baseline abnormal values had significant improvements in their mean systolic blood pressure, blood glucose, high-density lipoprotein and triglyceride levels, diet, and physical activity during the three-year follow-up.

The prevalence of the different CVD risk factors in SLE patients ranges between 20–50% for hypertension, 3–9% diabetes, 9–15% dyslipidemia, 15–38% smoking, and 16–22% metabolic syndrome (compared to 5–6% in general population) (11–14). Despite the increased prevalence of CVD risk factors in SLE patients, many lupus patients are not aware of their increased risk of CVD, and they do not receive routine screening and counseling for CVD risk factors (15–19). Our study confirms that SLE patients generally do not perceive “lupus” as a CVD risk factor, as only 22% of our patients who completed the baseline survey were aware of their lupus-associated CVD risk.

Cardiovascular disease prevention programs help patients increase their awareness of CVD risk factors. However, these programs, especially in the setting of rheumatology practices are

not common and only less than one-quarter of SLE patients receive appropriate preventive care (20). Thus, CVD screening and/or counseling is not globally addressed by rheumatologist; a critical point especially given that many lupus patients perceive their rheumatologists as their primary care physicians. O'Neill *et al.* implemented a patient care protocol mandating regular assessment of CVD risk factors in their lupus clinic, which resulted in the discussion of CVD risk factors with more than 90% of the patients; 47% of the smokers reduced or stopped smoking, but data on effect on others CVD risk factors were not reported (21). One program in Canada randomized 141 lupus patients to receive an individualized program for CVD risk reduction versus standard care; there was a significant decrease in the Framingham eight-year CVD risk calculation at one year in the first group of patients (22). Another United Kingdom program studied 56 lupus patients over a three-year period in a nurse-led coronary heart disease clinic; there were improvements in number of patient with acceptable or ideal blood pressure and in lipid levels (TG and LDL) (23–24). Our program is the first three-year CVD counseling program that was offered as part of the standard lupus care; we have demonstrated that selected CVD risk factors can be modified with continuous counseling in lupus patients.

In our program, significant improvements in blood pressure, blood glucose and cholesterol profile were observed only in patients with abnormal values at baseline, i.e., high-risk patients. Given that the clinical significance of a decreasing blood pressure, blood glucose, or cholesterol values in those patients with normal baseline values is unknown, we believe that the lack of improvement in the overall population is acceptable. Furthermore, it is unlikely that the regression to the mean contributed to our observations due to: a) relatively high number of patients with abnormal baseline CVD risk factors (except high glucose); and b) the low probability of untreated CVD risk factors improving spontaneously over time. Although there was no significant decrease in the BMI, it is important to note that patients were able to maintain their weight constant, many despite corticosteroid treatment. Although clinically significant improvement of the CVD risk factors was the primary objective of the counseling, our program should be considered also as a quality improvement initiative with a focus on counseling and lifestyle modifications, with an ultimate goal of helping decrease global CVD risk.

Diet has an important role in prevention of cardiovascular events. Davies *et al.* demonstrated that low glycemic index diet could achieve weight loss in SLE patients on low dose corticosteroid therapy (25). Based on our CVD- Prevention Counseling Program patients referred to the nutrition counseling, we previously reported that nutritional guidance using patient-centered methods reduce total calories, percent calories from total and saturated fat, and sodium intake in patients with SLE. Patients also reported significant increases in eating a diet rich in fruits and vegetables, a high-fiber diet, at least two servings of fish per week, and a low-cholesterol diet. Diet and nutrient modification was accompanied by reductions in weight and BMI (10). When the follow-up was extended to three years, we confirmed our previous observations; moreover, we believe that the benefit of increased physical activity on the cholesterol profile was reflected in the increase in mean HDL.

Urowitz *et al.* found early deaths of SLE patients are related to disease activity but late deaths are related to cardiovascular disease (26). Although the follow-up of cardiovascular

disease outcomes, e.g., stroke, myocardial infarction was not an objective of the program, we reported three deaths during the study period, and two were related to a cardiovascular disorder, which highlights the impact of CVD in the excess mortality rate of SLE compared to an age-matched general population.

Some lupus specialists believe that lupus, like diabetes mellitus, should be considered a coronary risk equivalent when evaluating patients for CVD risk stratification (20). The European League Against Rheumatism already recommends increasing the CVD risk score by a factor of 1.5 in patients with rheumatoid arthritis (27); a similar approach might be considered for lupus (28). As a result, preventive cardiology has been proposed to be an essential component of care for patients with lupus (18). We agree with the importance of preventive cardiology in lupus patients; our program demonstrates the importance of individualized face-to-face CVD counseling.

Limitations of our study include: a) half of the patients did not complete the three-year program; however, there was no difference between the baseline characteristics of those who completed and did not complete the program; b) we have no data on the number of patients who were referred to the counseling and the participation was voluntary, thus patients may not be representative of the entire SLE population; c) a controlled intervention study would have provided stronger data by strictly measuring the changes in response to the intervention; however, our program was originally designed as an optional standard of care education program with no medical intervention other than the counseling, and we wanted to determine the impact of a nurse practitioner-based education program in a clinical setting, rather than a research setting; d) we have not recorded lupus disease activity and premenopausal status, which can influence CVD risk; e) some of the data collected, e.g. diet habits and physical activity, were self-reported; f) some of the point estimates were moderate; thus some of the statistically significant values may not be clinically significant; g) the prevalence of selected CVD risk factors, e.g. diabetes, smoking, was relatively low resulting in potential lack of power to show statistical significance; and h) our study design did not allow us to generate quantified estimates of the maximum attributable population benefit of CVD prevention counseling in lupus patients.

In conclusion, our data suggest that a CVD prevention counseling program decreases the prevalence of CVD risk factors in SLE patients. Although we believe that CVD prevention counseling should be incorporated into routine lupus care, long-term follow-up of larger SLE cohorts will determine if the counseling decreases the incidence of CVD.

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SIGNIFICANCE AND INNOVATIONS

1. Despite decreasing mortality rates in systemic lupus erythematosus, cardiovascular disease (CVD) still remains the major cause of mortality.
2. Systemic lupus erythematosus patients generally do not perceive “lupus” as a CVD risk factor, as only 22% of our patients who completed the baseline survey were aware of their lupus-associated CVD risk.
3. Our program, the first three-year CVD prevention counseling program that was offered as part of standard lupus care, demonstrated that selected CVD risk factors can be modified with continuous counseling in lupus patients.

Table I

Baseline Characteristics of the Study Population (all patients, and comparison between patients who completed 3-year follow-up and who did not)

Baseline Characteristics	Total Population (n=121)	3-year Follow-up Completed (n=62)	3-year Follow-up Not Completed (n=59)	<i>P</i> *
Age, years	41.4 ± 13.7	42.7 ± 13.2	39.6 ± 14.2	0.2
Sex, Female	108 (89%)	55 (89%)	53 (88%)	0.84
Race				
White	58 (48%)	23 (37%)	35 (59%)	0.07
African-American	53 (44%)	34 (55%)	19 (32%)	0.03
Ethnicity				
Hispanic or Latino	38 (31%)	18 (29%)	20 (34%)	0.56
Autoimmune Disease				
SLE* without aPL/APS	92 (76%)	49 (79%)	43 (73%)	0.52
SLE* with aPL/APS	18 (15%)	9 (14%)	9 (15%)	1.00
SLE-like** with aPL/APS	11 (9%)	4 (6%)	7 (12%)	0.35
Comorbidities				
History of Hypertension	57 (47%)	35 (56%)	22 (37%)	0.03
History of Diabetes	14 (11%)	10 (16%)	4 (7%)	0.11
Hypercholesterolemia	26 (22%)	11 (18%)	15 (25%)	0.33
History of Smoking	27 (22%)	15 (24%)	12 (20%)	0.61
Current Smoking	8 (7%)	4 (27%)	4 (33%)	0.70
Metabolic syndrome	24 (20%)	15 (24%)	9 (15%)	0.22
Baseline Medications				
Antihypertensive Drugs	50 (41%)	32 (52%)	18 (30%)	0.41
Antidiabetes Drugs	8 (7%)	5 (8%)	3 (2%)	0.58
Cholesterol Lowering Drug	14 (11%)	7 (11%)	7 (12%)	0.39
Prednisone (anytime)	82 (68%)	32 (52%)	50 (83%)	0.002
Aspirin	33 (27%)	19 (31%)	14 (24%)	0.40
Other Antiplatelet Agent	3 (2%)	2 (3%)	1 (2%)	1.00
Warfarin	13 (11%)	7 (11%)	6 (10%)	0.84
LMWH	4 (3%)	3 (5%)	1 (2%)	0.62
Hydroxychloroquine	82 (68%)	46 (75%)	36 (62%)	0.12

aPL: antiphospholipid antibodies; **APS:** antiphospholipid syndrome; **LMWH:** low molecular weight heparin; **SLE:** systemic lupus erythematosus;

* American College of Rheumatology (ACR) SLE Classification Criteria 4 met; and

** ACR SLE Criteria only 3 met.

Table II

Change in Cardiovascular Disease (CVD) Risk Factors and Life Style Habits During the 3-year Follow-up in the Total Population:

	Change in Total Population (n: 121)
CVD RISK FACTORS	
Abnormal Blood Pressure (%)	1.00 (0.98–1.02)
– Systolic BP (mean)	+ 1.44±1.4
– Diastolic BP (mean)	+ 0.22±1.1
Abnormal Blood Glucose (%)	1.11 (1.08–1.15) ***
– Blood Glucose (mean)	1.44±2.2
Abnormal Lipid Profile (%)	0.99 (0.97–1.01)
– Total Cholesterol (mean)	– 2.88±2.9
– LDL (mean)	– 3.24±2.5
– HDL (mean)	+ 21.6 (0.72) *
– Triglyceride (mean)	– 6.12±3.9
Abnormal Body Mass Index (%)	1.03 (0.98–1.08)
– Body Mass Index (mean)	+ 0.72±0.7
Current Smoking (%)	0.94 (0.86–10.2)
LIFE STYLE HABITS	
Poor Diet Habits (%)	0.94 (0.93–0.96) ***
– Rich Fruit/Vegetables	1.06 (1.03–1.08) ***
– Rich Grain/Fiber	1.06 (1.04–1.08) ***
– Fish Twice/week	1.03 (1.01–1.05) **
– Alcohol Not > 1 Drink/day	1.06 (1.01–1.11) *
– Cholesterol Free Diet	1.02 (1.01–1.04) **
Poor Physical Activity (%)	0.94 (0.92–0.96) ***
– Exercise 30 min/day	1.04 (1.02–1.06) ***
– Exercise 60 min/day	0.98 (0.96–1.01)

Comparison was made by using linear mixed effect regression model. The estimation of difference between groups was expressed with Odds Ratio (95% Confident Interval) for categorical variables, and with regression coefficient (Standard Error) for continuous variables.

*
p<0.05;

**
p<0.001;

p<0.0001.

BP: blood pressure; **CVD:** cardiovascular disease; **DBP:** diastolic blood pressure; **HDL:** High-density lipoprotein; and **LDL:** Low-density lipoprotein.

Change in Cardiovascular Disease (CVD) Risk Factors and Life Style Habits During the 3-year Follow-up in Subgroups of Patients with Abnormal Baseline Values

# of Patients with Abnormal Baseline Values						
	Blood Pressure (n:50)	Glucose (n:7)	CHL Profile (n:82)	BMI (n:77)	Diet (n:100)	Exercise (n:95)
CVD RISK FACTORS						
Abnormal Blood Pressure (%)	0.94(0.92–0.96)***	0.96(0.9–1.0)	0.99(0.97–1.0)	1.0(0.98–1.0)	1.0(0.98–1.0)	1.0(0.98–1.0)
– Systolic BP (mean)	– 6.12±2.16*	– 2.16±4.3	+2.2±1.8	+4.30±2.2	+3.60±1.8	+3.24±1.8
– Diastolic BP (mean)	– 2.16±1.44	– 0.72±3.6	+0.1±0.01	+0.36±1.1	+0.36±1.1	+0.36±1.1
Abnormal Blood Glucose (%)	1.09(1.05–1.1)***	NA	1.1(1.06–1.1)***	1.1(1.06–1.1)***	1.08(1.05–1.1)***	1.1(1.07–1.1)***
– Blood Glucose (mean)	– 0.36±3.24	– 42.1±19.8*	– 0.1±2.2	+0.36±2.5	– 0.3±2.2	+0.04±2.2
Abnormal Cholesterol Profile (%)	1.0(0.97–1.1)	No	0.9 (0.92–0.96)***	0.98(0.96–1.0)	1.0(0.98–1.0)	1.0(0.98–1.0)
– Total Cholesterol (mean)	0.14±5.4	+11.16±13.7	+1.44±3.6	+0.72±2.9	– 1.44±3.2	+2.52±3.2
– LDL (mean)	– 3.24±4.68	+5.0±7.9	– 1.08±3.6	– 0.52±0.5	– 1.80±2.5	+1.08±2.5
– HDL (mean)	+2.52±1.08	– 0.7±6.8	+ 5.4 ± 0.36***	+ 6.5 ± 0.36***	+1.08±1.1	+1.08±1.1
– Triglyceride (mean)	– 3.6±6.48	+36.4±33.8	– 12.6 ± 5.4*	– 10.0±4.3	– 7.20±4.7	– 2.16±4.7
Abnormal Body Mass Index (%)	1.0(0.97–1.1)	0.94(0.84–1.0)	1.0(0.98–1.1)	0.93(0.95–1.2)	1.0(0.97–1.1)	1.0(0.98–1.1)
– Body Mass Index (mean)	+0.18±0.36	– 3.2±0.7***	– 0.22±0.2	– 0.36±0.3	– 0.11±0.3	– 0.14±0.3
Current Smoking (%)	0.95(0.8–1.1)	NA	0.97(0.89–1.1)	0.99(0.91–1.1)	0.95(0.87–1.1)	0.95(0.87–1.0)
LIFE STYLE HABITS						
Poor Diet Habits (%)	0.95(0.93–0.97)**	0.92(0.95–1.0)	0.94(0.92–0.96)***	0.94(0.9–0.96)***	0.93(0.9–0.96)***	0.94(0.9–0.96)***
– Rich Fruit/Vegetable (%)	1.08(1.04–1.1)***	1.1(0.99–1.2)	1.07 (1.04–1.1)***	1.05(1.02–1.1)***	1.06(1.04–1.1)***	1.06(1.03–1.1)***
– Rich Grain/Fiber (%)	1.06(1.04–1.1)***	1.1(0.99–1.2)	1.06 (1.04–1.1)***	1.07 (1.04–1.1)***	1.07(1.05–1.1)***	1.06(1.04–1.1)***
– Fish Twice/Week (%)	1.0(0.99–1.0)	1.0(0.95–1.1)	1.03(1.01–1.05)**	1.04(1.01–1.06)**	1.04(1.02–1.1)***	1.03(1.01–1.05)***
– Alcohol Intake 1/day (%)	1.13(1.02–1.2)*	NA	1.06(1.01–1.13)*	1.05(0.99–1.1)	1.05(1.0–1.1)	1.01(0.99–1.1)

# of Patients with Abnormal Baseline Values						
	Blood Pressure (n:50)	Glucose (n:7)	CHL Profile (n:82)	BMI (n:77)	Diet (n:100)	Exercise (n:95)
– Cholesterol Free Diet (%)	1.0(0.98–1.0)	NA	1.02(0.99–1.1)	1.03(1.01–1.05)*	1.03(1.01–1.05)**	1.03(1.01–1.05)**
Poor Physical Activity (%)	0.94(0.92–0.97)***	0.93–0.86–1.0)	0.94(0.92–0.96)***	0.95(0.9–0.96)***	0.94(0.9–0.96)***	0.93(0.9–0.95)***
– Exercise 30min/day	1.04(1.02–1.1)**	1.0(0.96–1.1)	1.04(1.02–1.06)**	1.04(1.02–1.07)**	1.05(1.03–1.1)***	1.05(1.03–1.1)***
– Exercise 60min/day	0.96(0.93–0.99)*	NA	0.98(0.95–1.0)	0.97(0.94–1.1)	0.99(0.93–1.0)	1.01(0.98–1.1)

Comparison was made by using linear mixed effect regression model controlling for age, gender, race, BMI, BS, diet habits, physical activity, and abnormal cholesterol profile abnormalities at baseline.

*
p<0.05;
**
p<0.001;

p<0.0001.

BP: blood pressure; **BMI**: body mass index; **BS**: blood sugar; **CHL**: cholesterol; **CS**: corticosteroid; **CVD**: cardiovascular disease; **HDL**: High-density lipoprotein; and **LDL**: Low-density lipoprotein.