The effects of life style modification on intraabdominal fat and carotid intima-media thickness in type 2 diabetes

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ABSTRACT

The effects of life style modification on intraabdominal fat and carotid intima-media thickness in type 2 diabetes

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(Directed by Professor Hyun Chul Lee)

Cardiovascular event is the most common cause of death in diabetic patients. So prevention and control of cardiovascular disease is the main stream to treat diabetic patients. There are many methods to control diabetes such as diet, exercise, insulin, and oral agents. But there are few reports that show the effects of life style modification (LSM) such as diet and exercise on atherosclerosis in type 2 diabetic patients. High-resolution B-mode ultrasound is well established as a non-invasive method for assessing arterial intima-media thickness (IMT) and carotid IMT is well related to clinically manifested

cardiovascular disease. The aim of this study was to investigate the effects of LSM on the progression of atherosclerosis by measuring carotid IMT in type 2 diabetic patients. A total 63 subjects with type 2 diabetes were recruited (control; n=24, LSM; n=39). After 6 months short term but strict LSM, there were significant difference in the changes of mean IMT between control and LSM group (0.13±0.23 mm vs. -0.05±0.16 mm, P=0.001). In the LSM group, the mean IMT decreased from 0.72±0.16 mm to 0.67±0.12 mm (P=0.062) without statistic significance whereas it increased from 0.66±0.20 to 0.80±0.19 mm (P=0.010) significantly in control group. After 6 months of LSM, the LSM group showed significant improvement in glycemic control and anthropometric parameters compared with control group. There were no significant difference in the changes of lipid profile, intraabdominal fat depth (IAD), and highly-sensitive C-reactive protein (hs-CRP). In conclusion, 6 month short term but strict LSM can delay the progression of atherosclerosis measured with IMT in type 2 diabetes even though there was no effect in the changes of lipid profile. The benefits of LSM on IMT is well correlated with improvement of glycemic control and anthropometric parameters but without changes of lipid profile or inflammatory parameter, hs-CRP.

Key words : type 2 diabetes, life style modification, intima-media thickness

I. INTRODUCTION

Diabetes mellitus is a disease of metabolic dysregulation, most notably abnormal glucose metabolism, accompanied by characteristic long term complications such as retinopathy, nephropathy, neuropathy, and vasculopathy [1]. Diabetes has an overall prevalence of 12.3% in U.S.A and the incidence is increasing annually including Korea [2, 3]. Among these complications, cardiovascular disease is the most common cause of death in diabetic patients [1]. Increased prevalence of cardiovascular disease in diabetes is preceded by a constellation of risk factors including dyslipidemia, hypertension, and obesity [4, 5]. These risk factors, together with hyperglycemia itself, act in concert to make a very potent atherogenic situation in diabetes [6], making catastrophic results, such as acute myocardial infarction or stroke. In addition, inflammatory cytokine such as high sensitivity C-reactive protein (hs-CRP) has also important roles in progression of atherosclerosis [7-10]. Tight glycemic control, weight loss, improvement of insulin resistance, and the correction of dyslipidemia contribute to the prevention of atherosclerosis in diabetic patients [11, 12].

In non-diabetic patients, there are a few reports about the benefits of life style modification (LSM) on atherosclerosis [13, 14]. But in type 2 diabetes, there

are few reports about the benefits of LSM with intensive diet control and exercise on atherosclerosis.

High-resolution B-mode ultrasound is a well established, non-invasive method for assessing arterial intima-media thickness (IMT) [15]. Carotid IMT is known to be correlated well with clinically manifested cardiovascular disease such as cerebral, peripheral, and coronary artery disease [12, 16].

The aim of this study was to investigate the effects of LSM on the progression of atherosclerosis by measuring carotid IMT in type 2 diabetic patients, with regard to variable factors which significantly influences atherosclerosis, such as, the degree of glycemic control, lipid profile, anthropometric changes, insulin resistance, and inflammatory cytokine. The findings in this paper shows that short-term but strict LSM attenuates the progression of atherosclerosis and the importance of strict LSM in type 2 diabetes.

II. MATERIALS AND METHODS

1. Subjects

A total of 63 subjects with type 2 diabetes were recruited from the outpatient clinic at Severance Hospital from September 2003 to September 2004. Diabetes was defined according to the American Diabetes Association diagnostic criteria [17]. The inclusion criteria were as follows: (1) No insulin therapy for glycemic control regardless of the use of oral hypoglycemic agent or exercise and diet treatment (2) HbA1c value ranging from 7.0% to 11.0%, and no medication changes in the last three months. Exclusion criteria were as follows: (1) Severe chronic disease including serious cardiovascular disease such as, ischemic cardiovascular disease, congestive heart failure, peripheral artery occlusive disease except hypertension, malignancy, chronic renal failure, and severe proliferative diabetic retinopathy (2) Positive for GAD (glutamic acid decarboxylase) antibody (3) A history of ketoacidosis.

2. Methods

A. Life style modification

During the 1 year follow-up, physicians were asked not to change nonessential drugs in medication and dosage that might affect glycemic control and lipid profile. Any essential medication changes were implemented

and then reported to the investigators. Before random assignment to the treatment groups, all patients received general diabetes education. After randomization, the subjects in the intervention group began a total of 12 month LSM program. This was composed of 3 months LSM program education and then monthly meetings for reinforcement on LSM for the next 9 months. For the first 3 months, the intervention group took part in education about diet and exercise weekly. The therapeutic goal of the education program was 7 % reduction of body weight and more than 3 hours of exercise per week. Two skilled nurses and one exercise trainer accomplished the program by one to one or two to one education with the participants. Every participants were closely monitored by the educator weekly at the meeting and were also self-monitored with the appropriate tools, such as recording the calorie of daily intake and the time of daily exercise

B. Metabolic parameters

To determine the relationship between LSM and IMT, and to evaluate which factors are influenced by LSM and contribute to IMT, various parameters were investigated. Blood samples were collected after 12 hours of fasting. Fasting plasma glucose (FPG), 2 hour postprandial plasma glucose (2PPG), HbA1c, insulin, C-peptide, total cholesterol, triglyceride, and HDL-

cholesterol levels were measured. LDL-cholesterol level was calculated using the Friedewald formula [18]. We measured anthropometric parameters including waist and hip circumference, weight, height and then calculated BMI. To assess the degree of insulin resistance, we calculated $HOMA_{IR}$ (homeostasis model assessment of insulin resistance) from the following formula ; fasting insulin level (μu/mL) × fasting glucose level (mmol/L) / 22.5 [19]. As a representative marker of systemic inflammation, hs-CRP was measured.

C. Intraabdominal fat depth

The distribution of abdominal fat was measured by ultrasonography with slight modification of the previous methods [20, 21], using ultrasonography (SA 9900, Medison, Korea). Intraabdominal fat depth (IAD) was defined as the distance between abdominal aorta to abdominal muscle. Intraobserver reliability was 1.4% and interobserver reliability was 1.9%.

D. Intima-media thickness

Carotid IMT was measured with high resolution B-mode ultrasonography (LOGIQ 9, GE medical system, Milwaukee, WI, USA) using 10 MHx linear probe (axial resolution 0.2mm) by Pignoli [22]. IMT was defined as the distance from intimal-luminal interface to medial-adventitial interface. The IMT was

measured at points of 2, 2.5 and 3 cm proximal to the flow divider on the far wall of the both common carotid arteries at the end of the diastolic phase. Intra-observer reliability was 7%. The data were interpreted with computer program (Intima Scope, media cross Co. Ltd, Osaka, Japan) by a single reader. Every plaque was excluded from interpretation. Intra-reader reliability was 5.5%.

E. Statistic analysis

The statistical analysis was performed using SPSS statistical analysis program (ver. 12.0, SPSS Inc., Chicago, IL, USA). Values are expressed as mean±S.D. Data were analyzed by independent t test, paired t test and Pearson's correlation test. A *P* value of less than 0.05 was considered to be statistically significant.

III. RESULTS

1. Baseline characteristics between LSM group and control group

There was no difference in the baseline characteristics between control group (n=24) and LSM group (n=39) in age, sex, duration of diabetes, smoking, anthropometric parameters, metabolic parameters (including FPG, 2PPG level, and HbA1c etc), IAD, hs-CRP, and IMT of common carotid artery (Table 1).

Table 1. Baseline clinical and metabolic characteristics of patients between control and LSM group.

	Control	LSM	*P*
N	**n=24**	**n=39**	
Age (yrs)	**54.83 ± 8.94**	**53.87 ± 7.85**	**0.656**
Sex(M:F)	**8:16**	**9:30**	
DM duration (yrs)	**11.38 ± 6.31**	**8.72 ± 9.94**	**0.247**
Smoker (%)	**34%**	**13%**	
Weight (kg)	**69.37 ± 23.56**	**66.27 ± 12.38**	**0.496**
Height (cm)	**159.08 ± 7.67**	**159.33 ± 6.66**	**0.899**
Waist circumference (cm)	**89.73 ± 11.75**	**87.61 ± 8.95**	**0.424**
Hip circumference (cm)	**100.38 ± 9.46**	**98.11 ± 6.29**	**0.308**
BMI (kg/m^2)	**25.90 ± 4.22**	**25.60 ± 3.62**	**0.765**
FPG (mg/dl)	**168.21 ± 33.19**	**160.00 ± 38.94**	**0.394**
2PPG (mg/dl)	**253.83 ± 68.20**	**219.38 ± 58.88**	**0.038**
HbA1c (%)	**8.69 ± 1.28**	**8.19 ± 1.46**	**0.179**
Total cholesterol (mg/dl)	**190.46 ± 35.10**	**196.03 ± 37.53**	**0.560**
Triglyceride (mg/dl)	**165.04 ± 96.15**	**161.49 ± 136.12**	**0.911**
HDL-cholesterol (mg/dl)	**47.5833 ± 6.48**	**58.51 ± 52.11**	**0.312**
LDL-cholesterol (mg/dl)	**120.88 ± 34.56**	**129.67 ± 30.89**	**0.299**
$HOMA_{IR}$	**2.46 ± 1.49**	**2.70 ± 1.42**	**0.547**
BUN (mg/dl)	**18.14 ± 14.46**	**15.24 ± 4.60**	**0.249**
Cr (mg/dl)	**0.92 ± 0.20**	**0.84 ± 0.16**	**0.063**
Protein (g/dl)	**7.14 ± 0.40**	**7.20 ± 0.38**	**0.539**
Albumin (g/dl)	**4.40 ± 0.32**	**4.46 ± 0.20**	**0.407**
hs-CRP (mg/L)	**1.09 ± 0.94**	**1.13 ± 1.48**	**0.910**
LP(a) (mg/dL)	**12.57 ± 10.00**	**18.41 ± 15.73**	**0.120**
C-peptide (ng/ml)	**1.35 ± 0.62**	**1.34 ± 0.39**	**0.899**
Insulin (μU/ml)	**31.75 ± 41.70**	**36.56 ± 60.81**	**0.734**
IAD (mm)	**61.60 ± 23.51**	**52.15 ± 20.45**	**0.108**
mean IMT (mm)	**0.66 ± 0.21**	**0.72 ± 0.16**	**0.259**

Datas are mean±S.D., FPG; fasting plasma glucose, 2PPG; 2 hour postprandial plasma glucose, BMI; body mass index, hs-CRP; highly sensitive C-reactive protein, IMT; intima-media thicknes

2. Changes in serum glucose level and HbA1c before versus after 6 months of LSM

There was significant changes in FPG (-21.10±31.20 mg/dL vs. 5.67±44.18 mg/dL, P=0.013), 2PPG (-26.15±54.35 mg/dL vs. 13.92±80.96 mg/dL, *P*=0.039), and HbA1c (-0.73±1.22% vs. 0.06±1.27% *P*=0.017) in the LSM group compared with the control group (Figure 1). In the LSM group, FPG level decreased from 160.00±8.90 mg/dl to 138.90±31.48 mg/dL ($p<0.001$), 2PPG levels decreased from 219.38±58.9 mg/dL to 193.23±52.68 mg/dL ($p<0.001$), and HbA1c decreased from 8.19±1.46% to 7.47±0.89% ($P<0.000$). In the control group, FPG level increased from 168.21±33.20 mg/dL to 173.88±47.94 mg/dL (*P*=0.536), 2PPG levels increased from 253.83±68.20 mg/dL to 267.75±76.51 mg/dL (*P*=0.408), HbA1c increased from 8.69±1.28% to 8.75±1.32% (*P*=0.812) but none of them showed statistical significance (Figure 2).

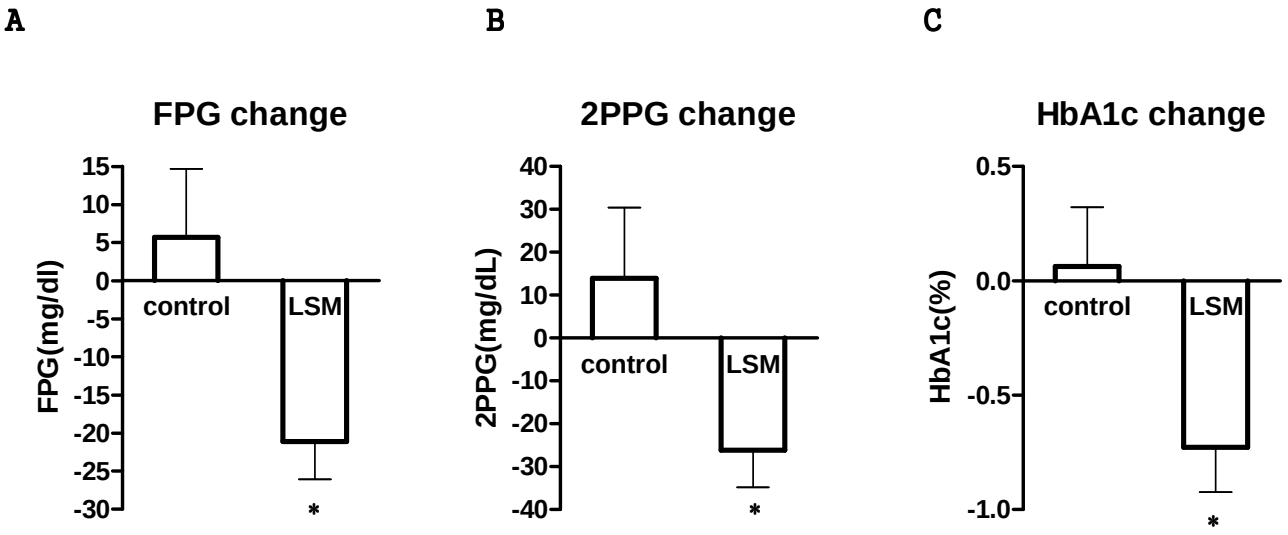
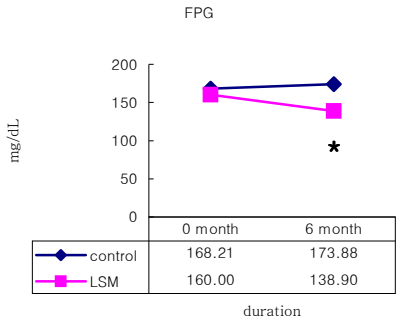


Figure 1. Comparison of changes in FPG, 2PPG, and HbA1c before vs. after 6 month LSM between control and LSM group A; Comparison of changes in FPG, B; Comparison of changes in 2PPG, C; Comparison of changes in HbA1c, *; P <0.05

A



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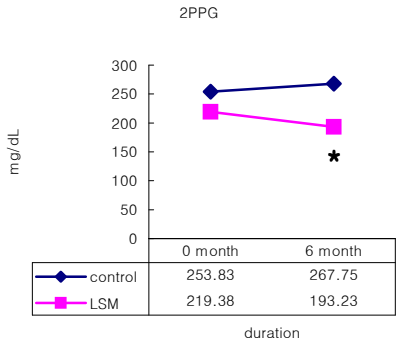

C

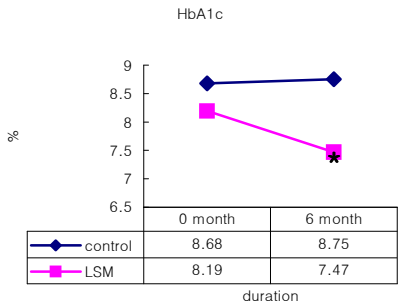

Figure 2. The changes of FPG, 2PPG, and HbA1c before and after 6 months LSM A; FPG changes, B; 2PPG changes, C; HbA1c changes, *; P <0.05

3. Changes in plasma lipid profile before versus after 6 months of LSM

There were no significant changes in lipid profile including total cholesterol, triglyceride, HDL-cholesterol, and LDL-cholesterol levels in both groups before versus after 6 months LSM. There was also no significant difference in the changes of plasma lipid profie between the two groups (Table 2).

Table 2. Changes in plasma lipid levels before versus after 6 months of LSM

	Control			LSM			P among
	baseline	6 months	p	baseline	6 months	p	groups
TC (mg/dl)	190.46 ± 35.10	186.92 ± 35.34	0.516	196.03 ± 37.53	192.41 ± 29.61	0.416	
Δ	3.54 ± 26.28			3.6154 ± 4.39			0.992
TG (mg/dl)	165.04 ± 96.15	222.00 ± 306.37	0.263	161.49 ± 136.12	138.56 ± 62.09	0.316	
Δ	-57.17 ± 244.10			22.92 ± 22.56			0.103
HDL-C (mg/dl)	47.58 ± 6.48	47.88 ± 10.41	0.862	58.51 ± 52.11	51.23 ± 12.49	0.413	
Δ	-0.29 ± 8.13			7.28 ± 8.79			0.506
LDL-C (mg/dl)	120.87 ± 34.56	112.88 ± 29.62	0.077	129.67 ± 30.89	122.50 ± 25.59	0.100	
Δ	8.00 ± 21.20			7.17 ± 4.25			0.897

Datas are mean±S.D., TC; total cholesterol, TG; triglyceride, HDL-C; high density lipoprotein-cholesterol, LDL-C; low density lipoprotein-cholesterol, Δ; difference between control and LSM group

4. Changes in anthropometric parameters and insulin resistance calculated from $HOMA_{IR}$ before versus after 6 months of LSM

Between the LSM group and the control group, the changes of body weight showed significant difference (1.80±2.47 kg vs. 0.00±1.66 kg, *P*=0.003) and waist circumference, hip circumstance, and BMI showed no difference between groups. In LSM group, body weight, waist circumference, hip circumference and BMI decreased significantly (body weight; 66.15±12.69 kg to 64.35±11.54 kg, *P*<0.001, waist circumference 87.5±9.17 cm to 84.38±9.37 cm, *P*<0.001, hip circumference; 98.07±6.42 cm to 96.65±6.61 cm, *P*<0.001, BMI; 25.83±3.90 kg/m^2 to 25.02±3.52 kg/m^2, *P* <0.001, respectively). In the control group, only the waist circumference showed statistic significance (from 89.73±11.75 cm to 87.44±12.5 cm, *P*<0.002). There was no statistic significance in the weight, hip circumference, and BMI in the control group. The changes of $HOMA_{IR}$ showed no significant difference between the two groups nor did it change significantly before and after the treatment (Table 3).

5. Intraabdomial fat depth before versus after 6 months of LSM

Between the two groups, there was no difference in the changes of IAD. In LSM group, IAD decreased significantly from 52.15±20.45 mm to 41.08±14.37 mm (*P*<0.001) and in the control group, IAD also decreased from 67.08±23.93 mm to 53.38±27.70 mm (*P*<0.001) (Table 3).

Table 3. Changes in anthropometric parameters, $HOMA_{IR}$, and IAD before and after 6 months LSM

	Control			LSM			p among
	baseline	6 months	p	baseline	6 months	p	groups
Weight (kg)	66.15 ± 12.70	64.35 ± 11.54	0.990	70.07 ± 23.84	70.07 ± 23.76	<0.001	
Δ	0 ± 1.66			-1.79 ± 2.47			0.003
Waist (cm)	87.50 ± 9.17	84.38 ± 9.37	0.002	89.73 ± 11.75	87.44 ± 12.50	<0.001	
Δ	2.29 ± 3.28			3.11 ± 4.18			0.418
Hip (cm)	98.07 ± 6.42	96.65 ± 6.62	0.815	100.38 ± 9.46	100.96 ± 13.97	<0.001	
Δ	-0.58 ± 2.47			1.42 ± 2.09			0.339
BMI (kg/m2)	25.83 ± 3.91	25.02 ± 3.52	0.322	26.33 ± 4.18	26.18 ± 4.21	<0.001	
Δ	0.15 ± 0.66			0.81 ± 1.02			0.014
$HOMA_{IR}$	129.67 ± 30.89	122.50 ± 25.59	0.195	2.20 ± 1.42	2.63 ± 1.51	0.762	
Δ	-0.66 ± 2.08			0.04 ± 1.47			0.166
IAD (mm)	61.08 ± 23.93	53.38 ± 27.7	0.003	52.15 ± 20.45	41.08 ± 14.4	<0.001	
Δ	0.00 ± 1.67			-1.79 ± 2.47			0.271

Datas are mean±S.D., BMI; body mass index, $HOMA_{IR}$; Homeostasis model assessment of insulin resistance, IAD; intraabdominal fat depth, Δ; difference between control and LSM group

6. Changes in hs-CRP before versus after 6 months of strict LSM

After 6 months of LSM, there was no significant difference between the two groups in the changes of hs-CRP although the LSM group showed significant decrease from 1.15±1.49 mg/dL to 0.69±0.86 mg/dL (P<0.001) and hs-CRP of the control group also decreased from 1.06±0.95 mg/dL to 0.84±0.76 mg/dL without statistic significance (Table 4).

7. Changes in intima-media thickness of carotid artery before and after 6 months of LSM

In LSM group compared with control group, there was significant decrease in mean IMT (0.052±0.165 mm vs. –0.13±0.23 mm, P=0.001) (Figure 3). In the LSM group, the mean IMT decreased from 0.72±0.16 mm to 0.67±0.12 mm (P=0.062) but without statistic significance whereas it increased from 0.66±0.20 to 0.80±0.19 mm (P=0.010) with statistic significance in the control group (Table 4).

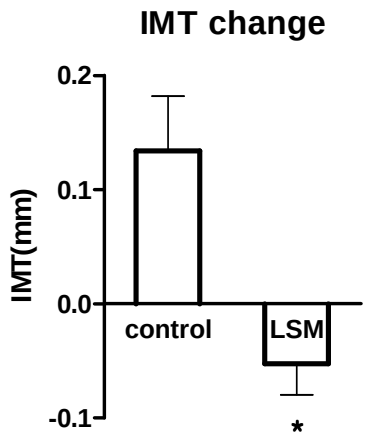

Figure 3. Comparison of the changes in mean IMT before versus after 6 monthsof LSM *; P <0.05

Table 4. Changes in hs-CRP and IMT before and after 6 months of LSM

	Control			LSM			p among
	baseline	6 months	p	baseline	6 months	p	groups
hs-CRP (mg/dL)	1.1 ± 0.95	0.84 ± 0.8	0.325	1.15 ± 1.49	0.69 ± 0.86	0.020	
Δ	0.22 ± 1.02			0.46 ± 1.09			0.414
IMT (mm)	0.66 ± 0.20	0.79 ± 0.19	0.010	0.72 ± 0.16	0.67 ± 0.12	0.062	
Δ	0.13 ± 0.23			-0.05 ± 0.16			0.001

Datas are mean±S.D., hs-CRP; highly sensitive C-reactive protein, IMT; intima-media thickness, Δ; difference between control and LSM group

IV. DISCUSSION

Previous studies showed that increased IMT was a good predictor of future cardiovascular event [23] and cardiovascular risk factors showed strong correlation with carotid atherosclerosis [23-26]. The Leiden Intervention Trial reported that diet, lipoprotein level, and the progression of coronary atherosclerosis was correlated closely in coronary heart disease patients [27]. Furthermore, in the Lifestyle Heart Trial, comprehensive life style changes for 1 year regressed severe coronary atherosclerosis even without the use of lipid-lowering drugs in coronary heart disease patient [28-30]. But there has been no definite report about the effect of LSM on atherosclerosis in type 2 diabetic patients.

Our study results showed that after 6 months of LSM, the changes in mean IMT between the LSM group and the control group showed significant difference (-0.05±0.16 mm vs. 0.13±0.23 mm , P=0.001). Although there was no statistic significance, mean IMT decreased from 0.72±0.16 mm to 0.67±0.12 mm (P=0.062) in LSM group, and increased from 0.66±0.20 mm to 0.80±0.19 mm (P=0.010) in the control group with statistic significance. This suggests that 6 months of intensive LSM, even if short term, can regress atherosclerosis in type 2 diabetes. This is the first prospective case-controlled study about the relationship of LSM on atherosclerosis measured by carotid IMT in type 2 diabetes. To determine which factors are related with the changes of mean IMT significantly, we investigated the changes of variable parameters which could affect atherosclerosis and which could be influenced by LSM. The LSM group showed significant improvement in glycemic control and body weight compared with the control group. But there was no difference in changes of lipid profile, IAD, and insulin resistance calculated from $HOMA_{IR}$ between the LSM group and the control group. In the LSM group, the changes in inflammatory parameter, such as hs-CRP showed nonsignificant decrease in the treatment group.

UKPDS 35 reported that in patients with type 2 diabetes, the risk of diabetic complications was strongly associated with the degree of hyperglycemia [31]. There are many methods in treating hyperglycemia such as exercise, diet, insulin therapy as well as the use of various oral hypoglycemic agents. Diet and exercise have been known to be important protecting the diabetic patients from serious atherosclerosis complications. DPP study proved that lifestyle changes such as 7% weight loss and at least 150 minutes physical activity per week reduces the incidence of diabetes in people with impaired fasting glucose or impaired glucose tolerance [32]. But there are few studies about the benefits of LSM on glycemic control in established type 2 diabetic patients. Pilot study proposed that short time intensive LSM with nutrition and exercise decrease weight, fasting glucose, and HbA1c level in type 2 diabetic patients. In our study, the LSM group showed significant improvement in the changes of FPG, 2PPG, and HbA1C level by 21 mg/dl, 26mg/dl, and 8 % respectively after 6 months of strict LSM. This result is compatible with the previous studies showing that LSM improves glycemic control in type 2 diabetes patients. Furthermore IMT improvement in the LSM group compared with the control group is probably related to the improvement of glycemic control. To our knowledge, this is the first prospective controlled study which shows that 6 months of strict LSM can improve glycemic control in type 2 diabetic patients in Korean people. Furthermore, it shows that probably, by the tight glycemic control, LSM can improve atherosclerosis as shown with the improvement in the carotid IMT in type 2 diabetic patients [31]

Framingham Heart Study reports that hyperlipidemia increases the risk of coronary heart disease [33-35] and further studies show that atherosclerosis can be regressed by correction of hyperlipidemia [36-38]. There are many reports showing that LSM can improve lipid profile, in advance to improvement in atherosclerosis [6, 30, 39]. There are also some studies which show that LSM can be benefitable on IMT in non-diabetic patients [13, 40, 41]. But in diabetes, IMT can be

less consistently correlated with classical risk factors such as LDL-cholesterol. Edith D et al. reported that simvastatin use for 2 years reduced LDL-cholesterol levels significantly but there was no alteration in IMT in diabetic patients [42]. In our study, there was no significant difference in the changes of lipid profiles even though total cholesterol, triglyceride, HDL and LDL-cholesterol had a tendency to decrease in intervention group, whereas triglyceride and HDL-cholesterol had a tendency to increase and total cholesterol and LDL-cholesterol had a tendency to decrease in the control group. The possible reasons of no difference in changes of lipid profile after LSM could be because of the short intervention period than other studies, a period too short to influence lipid profile. Considering the tendency of the lipid levels in each group, long term LSM can result in a statistically significant data. The other reason for this could be the difference in the race and study design. Even though there is no difference in the changes of lipid profiles, mean IMT change has significant difference between groups, with a trend to regress in the treatment group compared to the significant increase in the control group. Consequently, LSM can delay the progression of atherosclerosis without lipid profile improvement after short term LSM in type 2 diabetes. For accurate decision whether LSM has any benefit on lipid profile and whether it has any relationship with the regression of atherosclerosis in type 2 diabetes, it is necessary to continue this project for a longer time. We plan to report the 1 year follow up data later on.

Insulin resistance is a risk factor of coronary heart disease [12, 43]. There are many reports proving the relationship between insulin resistance and obesity by measuring waist circumference and BMI [11]. In our study, we measured body weight, height, waist and hip circumference, and then calculated BMI. As a laboratory parameter of insulin resistance, we calculated $HOMA_{IR}$. Between the groups, the changes of body weight and BMI showed significant difference. In the LSM group, body weight, waist and hip circumference and BMI decreased

significantly. In the control group, waist circumference decreased while others had no significant changes. Improvement of such anthropometric parameters in the intervention group implies improvement of insulin resistance. Therefore, we can guess that LSM has beneficial impacts on insulin resistance. But in our data, one of the parameters in insulin resistance, $HOMA_{IR}$ showed discrete result. $HOMA_{IR}$ is a method of assessing β-cell function and insulin resistance from basal glucose and insulin levels [44]. Assessing insulin resistance, $HOMA_{IR}$ is known to be closely correlated with insulin resistance index assessed by euglycemic clamp [19]. In our study, many parameters concerning insulin resistance in LSM group were improved but there was no changes of $HOMA_{IR}$. There can be two possibilities for this. One is that LSM actually dose not contribute to the improvement of insulin resistance regardless of the improvement of anthropometric parameters which have been considered to have benefits in insulin resistance. Another is that $HOMA_{IR}$ may not reflect the real β-cell function because of the long diabetes duration and lean body mass in our subjects[45]. IAD (intra-abdominal fat depth) is an indicator of visceral fat. There are many reports on the influence of visceral fat on insulin resistance and its correlation with obesity, diabetes, atherosclerosis [46, 47]. Liu et. al. reported that visceral fat measured with ultrasound showed significant association with carotid IMT [48]. We hypothesized that LSM could reduce visceral fat, represented by IAD and that it can contribute to the regression of atherosclerosis represented with IMT in type 2 diabetic patients. After 6 months of LSM, there was no significant difference in the changes of IAD between groups even though both groups showed reduction of IAD significantly. And there was no correlation between IAD and IMT. This findings can be explained as follows. After enrollment of the subjects, we let the LSM group to participate in the education program twice a week. But for control group, we gave only the standard education like other diabetic patients. But for the compliance of follow up, even for control group, we did our best to explain the result of all tests at

every visit for clinic. We guess that the probable better insight of our control group subjects about their disease than general patients lead to weight reduction and consequently visceral fat reduction. Even though there is no difference in changes of visceral fat between groups, the changes of visceral fat in treatment group correlates significantly with the changes of HbA1c (r=0.345, P=0.040) and the changes of body weight (r=0.442, P=0.009). So carefully, we suggest that longer intervention time may lead to the difference in changes of visceral fat.

CRP is a hepatic acute phase protein regulated by circulating levels of interleuekin-6. IL-6 is an adiopokine secreted from adipose tissue. Obesity induces elevation of inflammatory cytokine, CRP from elevated IL-6 and TNF-α from adipose tissue and it is related with insulin resistance and diabetes[49]. Inflammation can be suggested to play an important role in diabetogenesis from the previous data that elevation of CRP and IL-6 can predict the prevalence of type 2 DM [50]. Furthermore it predicts coronary heart disease in diabetic subjects[51] and CRP has a strong association with acute coronary event [52]. In our data, there was no significant difference in changes of hs-CRP between groups even though the LSM group showed significant decrease of hs-CRP, whereas control group showed no significant changes. Interestingly, in the control group, hs-CRP showed significant correlation with the progression of IMT (r=0.438, P=0.047). This data is compatible with other studies that hs-CRP contributes to atherosclerosis. But the relationship between LSM and hs-CRP has been controversial [7, 53-57]. There is one report that short term LSM for 16 weeks with moderate to intense exercise improved insulin resistance but the changes were not associated with decreased inflammatory marker CRP, even if the subjects were stratified by their changes in fitness or obesity [10]. So it would be necessary to do long term follow up to evaluate the relationship between hs-CRP and IMT.

V. CONCLUSION

In conclusion, 6 month of short term but intensive LSM can delay the progression of atherosclerosis measured with IMT in type 2 diabetes even though there was no effect in the changes of lipid profile. The benefits of LSM is probably attributed to improvement of glycemic control and anthropometric parameters without the changes of lipid profile or inflammatory parameter hs-CRP.

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2형 당뇨병 환자에서 철저한 생활습관 조절이 복부 지방과 경동맥 내중막 두께에 미치는 영향

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강신애

당뇨병은 당 조절 대사에 불균형을 일으킴으로 인하여 동맥경화증 등의 만성 합병증을 유발하는 대사질환으로서 최근 들어서 유병률이 급격하게 증가하고 있다. 당뇨 환자에서 심장혈관질환은 가장 흔한 사망원인 중 하나이며 치료와 예방의 중요성이 강조되고 있다. 당뇨병을 치료하는 데 있어서 생활습관 조절의 필요성은 많이 강조되어 왔지만, 제 2형 당뇨병 환자에서 생활습관 조절이 동맥경화증의 지연에 미치는 영향에 대한 연구는 미미하다. 본 연구에서 6개월간의 짧지만 철저한 생활습관 조절 후에 대조군과 생활습관 조절군은 평균 경동맥 내중막 두께(이하 IMT)의 변화에서 의미 있는 차이를 나타내었다(0.13±0.23 mm vs. -0.05±0.16 mm, P=0.001). 6개월간의 생활습관 조절 후에 IMT는 대조군에서 0.66±0.21 mm에서 0.80±0.19 mm로 증가하였고(P=0.010), 생활습관 조절군에서 0.72±0.16 mm에서 0.67±0.12 mm로 감소하였다 (P=0.062). 6개월간의 생활습관 조절 후에 대조군과 비교시 치료군에서 혈당과 신체계측치의 변화에서 유의한 차이를 보였으며, 지질 지표, 복부 지방, hs-CRP 의 변화는 유의한 차이를 보이지는 않았다. 따라서 IMT의 유의한 변화는 혈당의 저하와 신체 계측치의 향상과 관련 있는 것으로 생각되며, 6 개월 간의 짧지만 철저한

생활습관 조절이 지질 지표의 변화를 일으키지는 못했지만 제 2형 당뇨병 환자에서 IMT를 감소시키고 나아가서 만성 합병증인 심장혈관 질환을 예방하는 데에 도움이 될 것으로 생각된다.

핵심되는 말: 제 2형 당뇨병, 생활습관 조절, 경동맥 내중막 두께