Association with mid-thigh low density muscle and LDL cholesterol subfraction size

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ABSTRACT

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Objective: Body fat accumulation is one of the important factors modifying the expression of small dense LDL(sdLDL). In adults, abdominal adiposity in particular has a close relationship with LDL particle size .
In this study, we investigated the relationship between mid-thigh low density muscle which represents fat components between and inside the muscle fibers measured by computed tomography (CT) and LDL cholesterol subfraction size in healthy women
Methods: A total of 237 healthy female were analyzed with questionnaire, anthropometric measurements, blood tests. Mid-thigh low density muscle mass areas were measured by computed tomography.
Results: Increased mid-thigh low density muscle mass significantly correlated with decreased LDL cholesterol subfraction size, independently of age and fat. Mid-thigh low density muscle areas by CT was positively correlated with BMI, waist, meanBP, HOMA-IR, TG, abdominal visceral fat areas, abdominal subcutaneous fat areas, mid-thigh fat areas after adjustment for age and fat.
Conclusion: The low-body intramuscular lipid seems to be a possible one of determinants of atherosclerosis in healthy women.

Key words : small dense low-density lipoprotein cholesterol, mid-thigh low density muscle, fat distribution

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I. INTRODUCTION

Obesity and an increased BMI has been associated with a high risk of cardiovascular disease[1]. Body fat distribution is also an important cardiovascular risk factor[2-4].

Several population studies support the fact that abdominal obesity is associated with increased blood pressure and plasma triglyceride (TG) levels[2,3]. Moreover, visceral fat accumulation is well recognized to be significantly related to the development of metabolic abnormalities, such as insulin resistance, type 2 diabetes, and dyslipidemia[5,6]. Several studies, on the other hand, has shown that lower body fat, as measured by thigh circumference, hip circumference or leg adipose tissue mass, is associated with a favorable metabolic profile. [7-13]. However, it is less clear the role played by intermuscular fat distributions.

Muscle area, measured by computed tomography (CT) can be divided into areas of normal and low attenuation muscle surface [14]. CT is a reliable method for assessing skeletal muscle lipid and reduced attenuation reflects a higher lipid content [15,16]. Many other studies have already shown that obesity and insulin resistance is strongly associated with increased areas of low attenuation muscle surface[14,17].

The importance of low-density lipoprotein (LDL) cholesterol concentration in coronary heart disease has been demonstrated in many studies. But most of all, the size of LDL particles represents an emerging cardiovascular risk factor since these particles can be associated with cardiovascular disease(CVD) independently of established risk factors, including plasma lipids. The predominance of small dense LDL (sdLDL) was also reported to be particularly atherogenic[14].

Body fat accumulation is one of the most important factors modifying the expression of sdLDL. In adults, abdominal adiposity in particular has a close relationship with LDL particle size[18]. However, information about sdLDL that have more atherogenic potential and its relationship with lower-body intramuscular fat is lesser known.

Therefore, we investigated the relationship between mid-thigh low density muscle which represents fat components between and inside the muscle fibers measured by computed tomography (CT) and LDL cholesterol subfraction size in healthy women.

II. SUBJECT AND METHODS

Subjects

We recruited 237 healthy women who visited the family medicine and obesity center at Sevrance Hospital. The study was approved by the Sevrance hospital and Ethics Committee, and written informed consent was obtained from all patients.

None of the subjects had a previous diagnosis or evidence of cardiovascular disease, diabetes, hypertension, Acute infectiouns disease or chronic inflammatory disease. In addition, we excluded pregnant women and subjects who had chronic renal disease, endocrine disease, cancer or medication usage

that could affect cardiometabolic function. All subjects completed a lifestyle questionnaire that included cigarette smoking and alcohol consumption.

Anthropometric measurements

Anthropometric measurements were taken with subjects in lightweight clothing and without shoes. BMI was calculated by dividing weight by height squared (kg/m^2). We measured waist circumference at the midpoint between the lower border of the rib cage and the iliac crest.

Metabolic parameters

Each subject had serum samples taken after an overnight fast. Fasting serum fasting glucose, total cholesterol, triglyceride and HDL-cholesterol levels using an ADVIA 1650 chemistry system (Bayer, Terrytown, NY, USA). LDL-cholesterol levels were calculated using the Friedewald equation. Lipoprotein particle sizes were determined using LipoPrint LDL system (Quantimetrix Corp., Redondo Beach, CA, USA). Fasting insulin was measured by a chemiluminescence immunoassay (Roche, IN, USA). Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) index [fasting insulin (units per milliliter) * fasting glucose (millimolar)/22.5]. Levels of high sensitivity C-reactive protein (hsCRP) were measured by a latex-enhanced immunoturbidimetric assay using an ADVIA 1650 Chemistry system (Bayer).

Regional fat distribution

Computed tomography(CT)

Abdominal adipose tissue areas were quantified by CT (Tomoscan 350;

Philips, Mahwah, NJ, USA). With the subject in a supine position, a 10-mm CT slice scan was acquired at the L4-L5 level to measure the total abdominal and visceral fat area. The visceral fat area was quantified by delineating the intra-abdominal cavity at the internal aspect of the abdominal and oblique muscle walls surrounding the cavity and the posterior aspect of the vertebral body. The subcutaneous fat area was calculated by subtracting the visceral fat area from the total abdominal fat area. A crosssectional scan of the same thickness was obtained for both legs at the midpoint between the anterior superior iliac crest and the patella, as described previously [15]. Skeletal muscle attenuation was determined by measuring the mean value of all pixels within the range of 0 to 100 Hounsfield units (HU). The mid thigh skeletal muscle area was compartmentalized into a normal density muscle area (+31 to +100 HU) and a low-density muscle area (0 to +30 HU).

Statistical analysis

All data were analyzed using the statistical program SAS 9.1 (SAS Institute, Cary, NC, USA). Analysis of covariance (ANCOVA) were performed to examine differences among groups and potential interactions . Data are described as the mean±SD in the case of normal distribution and as median and interquartile range in the case of non-normal distribution. After adjusting for age and BMI, Pearson's correlation coefficients were calculated to evaluate the relationship between mid-thigh low density muscle and variables. A step-wise multiple linear regression analysis was performed to clarify the factors contributing to mid-thigh low density muscle. Significance was defined as $P < 0.05$.

III. RESULTS

The clinical characteristics of the participants by mid-thigh low density muscle area are shown in Table 1. As mid-thigh low density muscle increased, there were significant progressive increase in BMI, waist circumference, glucose, HOMA-IR, TG, WBC, hsCRP, AST, ALT, visceral fat area, subcutaneous fat. Also, mean LDL size decreases as mid-thigh low density muscle increase (Table 1).

Table 1. Clinical characteristics and mid-thigh low density muscle of subject

Data are shown as means±SD. *p* Values were calculated by an ANOVA test.

	Total	Mid-thigh Low Density muscle 1	Mid-thigh Low Density muscle 2	Mid-thigh Low Density muscle 3	Mid-thigh Low Density muscle 4
Number	237	60	59	59	59
Age(years)	36.60±11.78	34.35±11.14	37.54±11.78	36.68±10.23	37.86±13.69
BMI(kg/m2)	27.12±5.03	24.58±4.29*†	25.35±3.64*	27.62±2.97*¶	30.96±6.08†§¶
Waist(cm)	89.77±9.31	84.57±7.76*†	86.22±7.52*	90.59±6.93*¶	97.73±8.96†§¶
Mean BP (mmHg)	91.47±42.78	97.60±84.80	87.94±9.38	89.29±9.88	91.23±9.08
Glucose(mg/dl)	92.14±12.75	89.69±10.75*†§	90.92±9.75*¶	92.68±8.25¶	95.27±19.03§¶
HOMA score	2.43±1.99	1.88±1.24*†§	2.08±1.49*†¶	2.55±1.95*§¶	3.23±2.73†§¶
Cholesterol(mg/dl)	186.33±36.13	177.13±32.49	191.0±35.55	184.93±34.97	192.52±40.08
TG(mg/dl)	99.64±55.20	77.03±32.06*	96.72±53.64*	98.74±47.20*	126.47±70.47†§¶
HDL(mg/dl)	53.90±13.24	57.44±13.19*†	54.66±11.13	52.57±16.52¶	50.86±10.71¶
LDL(mg/dl)	112.67±32.81	104.39±27.93	117.72±31.51	112.34±33.59	116.36±36.81
LDL subfraction(Å)	268.90±4.40	270.45±3.01*	269.59±3.39*	268.88±4.09*	266.66±5.77†§¶
WBC($10^3/\mu\ell$)	6.03±1.53	5.70±1.30*	5.88±1.54*	6.12±1.64	6.40±1.56§¶
hsCRP(mg/L)	1.51±2.01	1.04±1.03*	1.43±1.68*	1.51±1.65*	2.06±3.01†§¶
AST(IU/L))	20.72±10.63	18.25±6.01*	20.83±9.23*	20.81±11.20*	23.09±14.21†§¶
ALT(IU/L)	23.26±22.70	16.63±9.12*	23.42±21.84*	25.25±25.34*	27.91±28.76†§¶
Creatinine(mg/dl)	1.45±10.37	0.74±0.11	0.78±0.10	0.86±0.78	0.72±0.09
L45 visceral fat(cm^2)	88.46±38.13	66.60±26.05*†	79.44±28.97*	95.44±33.33*¶	112.38±45.40†§¶
L45 subcutaneous fat(cm^2)	265.58±90.45	228.743±62.27*	222.15±74.99*	270.76±77.53*	340.66±92.60†§¶

1:Mid-thigh low density muscle(cm^2)≤32.46, 2:Mid-thigh low density muscle(cm^2)>32.46 and ≤39.06, 3:Mid-thigh low density muscle(cm^2)>39.06 and ≤47.75, 4: Mid-thigh low density muscle(cm^2) >47.75

* $p < 0.05$ vs. mid-thigh muscle 4
† $p < 0.05$ vs. mid-thigh muscle 3
§ $p < 0.05$ vs. mid-thigh muscle 2
¶ $p < 0.05$ vs. mid-thigh muscle 1

Mid-thigh low density muscle areas by CT was positively correlated with BMI,

waist, HOMA-IR, TG, abdominal visceral fat areas, abdominal subcutaneous fat areas mid-thigh fat areas whereas it was negatively correlated with LDL subfraction size after adjustment for age and fat percentage (Table2) (Figure 1,2.).

Table 2. Correlation of mid-thigh low density muscle and variable

	Unadjusted		Age-adjusted		Age-and fat adjusted	
	r	p-value	r	p-value	r	pvalue
Age(years)	0.073	0.261	-	-	-	-
BMI(kg/m2)	0.524	<0.0001	0.514	<0.0001	0.327	<0.0001
Waist(cm)	0.578	<0.0001	0.581	<0.0001	0.393	<0.0001
Mean BP (mmHg)	-0.087	0.190	0.208	0.004	0.013	0.860
Glucose(mg/dl)	0.135	0.038	0.112	0.125	0.026	0.726
HOMA score	0.338	<0.0001	0.361	<0.0001	0.175	0.017
Cholesterol(mg/dl)	0.094	0.151	0.049	0.504	0.055	0.456
TG(mg/dl)	0.295	<0.0001	0.277	0.0001	0.153	0.037
HDL(mg/dl)	-0.194	0.003	-0.258	0.0003	-0.135	0.067
LDL(mg/dl)	0.080	0.225	0.045	0.537	0.056	0.452
LDL subfraction(Å)	-0.298	<0.0001	-0.257	0.0004	-0.168	0.023
WBC($10^3/\mu\ell$)	0.147	0.025	0.111	0.129	-0.022	0.771
hsCRP(mg/L)	0.201	0.002	0.221	0.002	0.025	0.733
meanPWV(cm/s)	0.014	0.834	-0.022	0.759	-0.112	0.130
L45 visceral fat(cm^2)	0.466	<0.0001	0.501	<0.0001	0.330	<0.0001
L45 subcutaneous fat(cm^2)	0.533	<0.0001	0.542	<0.0001	0.307	<0.0001

Coefficients (*r*) and *p* values are calculated by the Pearson correlation model.

Correlations between mid-thigh low density muscle and most biochemical parameters were no longer significant after adjustment for fat except for LDL subfraction size, HOMA and TG.

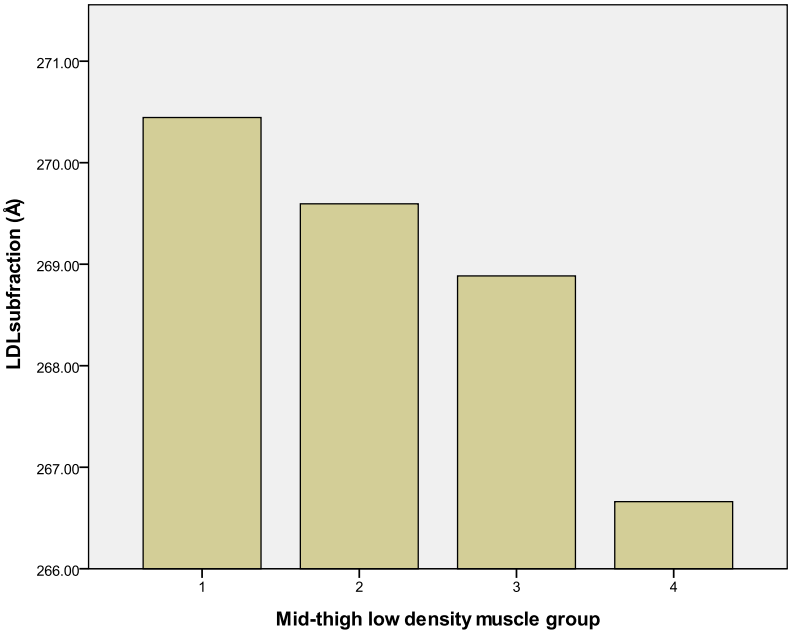

FIGURE 1: Relationship between mid-thigh low density muscle and LDL subfraction
1:Mid-thigh low density muscle(cm^2)≤32.46, 2:Mid-thigh low density muscle(cm^2)>32.46 and ≤39.06, 3:Mid-thigh low density muscle(cm^2)>39.06 and ≤47.75, 4: Mid-thigh low density muscle(cm^2) >47.75

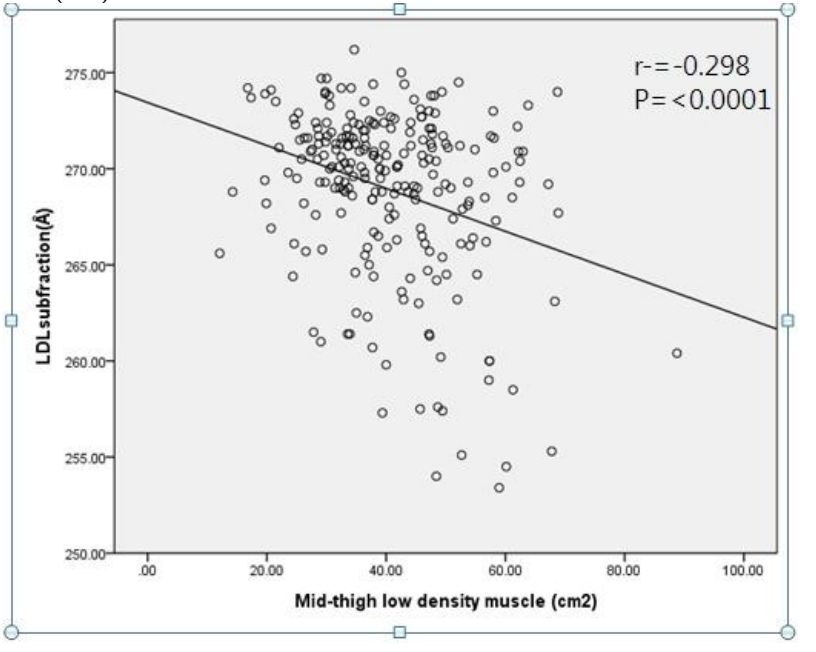

FIGURE 2: Relationship between mid-thigh low density muscle and LDL subfraction

Further, in step-wise multiple regression analysis, BMI and LDL subfraction size were selected as explanatory variables accounting for mid –thigh low density muscle areas. (Table 3).

TABLE 3. Step-wise multiple linear regression analysis of clinical variables associated with mid-thigh low density muscle as dependent variable

Variables	Model R^2	β coefficient	SE	F	p
BMI	(0.273)	1.103	0.142	60.70	<0.001
LDL subfraction	0.299	-0.447	0.163	7.48	<0.001

IV. DISCUSSION

The mid-thigh low density muscle which represents lipid-rich skeletal muscle has been shown to link obesity and insulin resistance[14,17]. The present study suggests that increased mid-thigh low density muscle mass significantly correlated with decreased LDL cholesterol subfraction size in women, independently of fat.

Computed tomography has the potential to distinguish different tissue types in vivo on the basis of their attenuation characteristics, which, in turn, are a function of tissue density and chemical composition[19]. Goodpaster et al. [20] showed that skeletal muscle attenuation by single-slice CT scans well demonstrate muscle fiber lipid content in percutaneous biopsy specimens. Further, accumulation of lipid within muscle is an aspect of regional fat distribution, which has recently gained considerable attention because of its association with insulin resistance. This was also shown to be strongly with insulin resistance independently of visceral adipose tissue[14]. While gluteofemoral fat, as measured by thigh circumference, hip circumference or leg adipose tissue mass, has a considerable and favorable association with a favorable metabolic profile [7-13], low attenuation muscle surface , a specific

component of fat-rich muscle measured by CT scan in the mid-thigh, has shown significantly correlates with apolipoprotein B and inflammatory markers[16].

Low-density lipoproteins(LDL) are composed of heterogeneous particles differing in density, size and chemical composition. The predominance of small dense LDL(sdLDL) was reported to be particularly atherogenic. Several mechanisms have been proposed to explain this association: their low affinity to the LDL receptor, low resistance to oxidative stress, prolonged plasma half-life, high binding affinity to surface components in the vessel wall and efficient penetration into the intima (Chait et al., 1993; Chapman et al., 1998; Brewer, 1999). LDL particle size is positively associated with triacylglycerol(TAG) and apolipoprotein B(apo B) concentrations, but negatively associated with high-density lipoprotein cholesterol(HDLC) concentration[21]. LDL diameter may improve the ability to predict CVD risk overuse of the classic lipid variables. Body fat accumulation is one of the important factors modifying the expression of sdLDL. Especially abdominal adiposity is reported to be associated with sdLDL in healthy men[18]. In obese youths, sdLDL is a common feature, and is associated with insulin resistance[22]. Several study shows that gluteofemoral fat is positively associated with LDL[7-13]. However, this relation has not been investigated with fat within skeletal muscle of lower body and sdLDL which is atherogenic lipoprotein.

Our results showed that increased mid-thigh low density muscle mass which represents lipid-rich skeletal muscle negatively correlated with LDL cholesterol subfraction size.

Denton and Randle [23] first described the existence of lipid storage in muscles in 1967. More than three decades later, the association between insulin resistance and triglyceride content measured in human muscle biopsy samples was initially reported by Pan et al.[24] who determined that muscle triglyceride content among non-diabetic Pima Indian men, an ethnic group with a pronounced disposition to obesity and T2DM, was related to insulin resistance

independent of total adiposity. Subsequent investigations utilizing biochemical determinations of muscle triglyceride content found similar associations[25-28].

The mechanisms of the linkage between fat accumulation and sdLDL were investigated in previous studies. Serum TG, especially very low-density lipoprotein (VLDL)-TG, was a major contributor to LDL particle size modification. In the Framingham Study, TG was the single most important factor affecting LDL particle size[29]. The relationship between LDL size and mid thigh low density muscle could be due to the connection with VLDL-TG.

There are several explanations for the lipid accumulation within skeletal muscle. Visceral fat is thought to release fatty acids into the portal circulation, where they may cause insulin resistance in the liver and subsequently in muscle. Another explanation is that the ability to store excess fat in adipose tissue is impaired, leading to the ectopic storage of fat into nonadipose tissue such as muscle and liver.

In our study, we show that this excess accumulation of fat into these cells is not only associated with insulin resistance[27, 30-32] and metabolic syndrome but also affects smaller LDL particle size which is more atherogenic lipoprotein.

The present study has several limitations. The cross-sectional design of the study does not allow clarification of any causal mechanisms. The small sample size is another limitation; a much larger population in a prospective clinical trial setting is required to better understand the lower body lipid rich muscle and sdLDL. Further studies are required to recognize relationship with the other atherosclerosis measurement tool like the carotid ultrasonography.

V. CONCLUSION

Our results suggest that increased low density muscle, a fatty component of the mid-thigh muscle, present smaller LDL subfraction size ,which is more atherogenic, on healthy women, independently of fat. This suggests that the role

of intramuscular lipid components associated with not only insulin resistance as known already , but also atherosclerotic factor. The low-body intramuscular lipid seems to be a possible one of determinants of atherosclerosis in healthy women.

REFERENCES

1.Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. N Engl J Med 1999; 341: 427–34.

2. Canoy D, Luben R, Welch A, Bingham S, Wareham N, Day N et al. Fat distribution, body mass index and blood pressure in 22 090 men and women in the Norfolk cohort of the European prospective investigation into cancer and nutrition (EPICNorfolk) study. J Hypertens 2004; 22: 2067–74.

3. Grundy SM, Adams-Huet B, Vega GL. Variable contributions of fat content and distribution to metabolic syndrome risk factors. Metab Syndr Relat Disord 2008; 6: 281–8.

4. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P et al. Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a casecontrol study. Lancet 2005; 366: 1640–9.

5. Nielsen S, Jensen MD. Obesity and cardiovascular disease: is body structure a factor? Curr Opin Lipidol 1997;8:200–4

6. Roust LR, Jensen MD. Postprandial free fatty acid kinetics are abnormal in upper body obesity. Diabetes 1993;42:1567–73

7. Seidell JC, Perusse L, Despres JP, Bouchard C. Waist and hip circumferences have independent and opposite effects on cardiovascular disease risk factors: the Quebec family study. Am J Clin Nutr 2001; 4: 315–21.

8. Terry RB, Stefanick ML, Haskell WL, Wood PD. Contributions of regional adipose tissue depots to plasma lipoprotein concentrations in overweight men and women: possible protective effects of thigh fat. Metabolism 1991; 40: 733–740.

9. Williams MJ, Hunter GR, Kekes-Szabo T, Snyder S, Treuth MS. Regional fat distribution in women and risk of cardiovascular disease. Am J Clin Nutr 1997; 65: 855–860.

10. Snijder MB, Visser M, Dekker JM, Goodpaster BH, Harris TB, Kritchevsky

SB et al. Low subcutaneous thigh fat is a risk factor for unfavourable glucose and lipid levels, independently of high abdominal fat. The health ABC study. Diabetologia 2005; 48: 301–8.
11. Buemann B, Astrup A, Pedersen O, Black E, Holst C, Toubro S et al. Possible role of adiponectin and insulin sensitivity in mediating the favorable effects of lower-body fat mass on blood lipids. J Clin Endocrinol Metab 2006; 91: 1698–1704.
12. Yim JE, Heshka S, Albu JB, Heymsfield S, Gallagher D. Femoralgluteal subcutaneous and intermuscular adipose tissues have independent and opposing relationships with CVD risk. J Appl Physiol 2008; 104: 700–7.
13. Sanae Tanaka, Bin Wu, Mari Honda, Kazuhisa Suzuki, Gen Yoshino, Keisuke Fukuo and Tsutomu KazumiJournal of Atherosclerosis and Thrombosis. 2011;18 , No. 5 365-72
14. Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE. Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. Diabetes 1997;46:1579–85.
15. Larson-Meyer DE, Smith SR, Heilbronn LK et al.; Look AHEAD Adipose Research Group. Muscle-associated triglyceride measured by computed tomography and magnetic resonance spectroscopy. Obesity (Silver Spring) 2006;14:73–87.16.
16. Marie-Christine Dubé, Simone Lemieux , Marie-Eve Piché , Louise Corneau , Jean Bergeron , Marie-Eve Riou et al. The Contribution of Visceral adiposity and Mid-Thigh Fat-Rich Muscle to the Metabolic Profile in Postmenopausal Women. obesity 2011; 19:953–9.
17. Simoneau JA, Colberg SR, Thaete FL, Kelley DE. Skeletal muscle glycolytic and oxidative enzyme capacities are determinants of insulin sensitivity and muscle composition in obese women. FASEB J 1995;9:273–8.
18. Lemieux I, Couillard C, Pascot A, Bergeron N, Prud'homme D, Bergeron J et al. The small, dense LDL phenotype as a correlate of postprandial lipemia in

men.Atherosclerosis. 2000 Dec;153(2):423-32
19. Bushberg JT, Seibert JA, Leidholdt EMJ, Boone JM. X-Ray computed tomography. In: Passano WM (eds). The Essentials of Medical Imaging. Williams et Wilkins: Baltimore, MD, 1994, 239–89.
20. Goodpaster BH, Kelley DE, Thaete FL, He J, Ross R: Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. J Appl Physiol 2000;89:104 –10
21. Kang HS, Gutin B, Barbeau P, Litaker MS, Allison J, Le NA., Low-density lipoprotein particle size, central obesity, cardiovascular fitness, and insulin resistance syndrome markers in obese youths, Int J Obes Relat Metab Disord. 2002 Aug;26(8):1030-5
22. Denton R, Randle P. Concentrations of glycerides and phospholipids in rat heart and gastrocnemius muscles. Effect of alloxan-diabetes and perfusion. Biochem J 1967: 104 (2): 416 - 22
23. Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, Bogardus C et al. Skeletal muscle triglyceride levels are inversely related to insulin action. Diabetes 1997: 46: 983-8.
24. Boden G, Lebed B, Schatz M, Homko C, Lemieux S., Effects of acute changes of plasma free fatty acids on intramyocellular fat content and insulin resistance in healthy subjects. Diabetes 2001: 50 (7): 1612 -7.
25. Oakes ND, Camilleri S, Furler SM, Chisholm DJ, Kraegen EW. The insulin sensitizer, BRL 49653, reduces systemic fatty acid supply and utilization and tissue lipid availability in the rat. Metabolism 1997:46 (8): 935 - 42.
26. Yu C, Chen Y, Cline GW, Zhang D, Zong H, Wang Y et al. Mechanism by which fatty acids inhibit insulin activation of insulin receptor substrate-1 (IRS-1)-associated phosphatidylinositol 3-kinase activity in muscle. J Biol Chem 2002: 277 (52): 50230 - 6.
27. Furler SM, Poynten AM, Kriketos AD, Lowy AJ, Ellis BA, Maclean EL et

al. Independent influences of central fat and skeletal muscle lipids on insulin sensitivity. Obes Res 2001: 9 (9): 535 -543.
28. McNamara JR, Jenner JL, Li Z, Wilson PW, Schaefer EJ. Change in LDL particle size is associated with change in plasma triglyceride concentration, Arterioscler Thromb. 1992 Nov;12(11):1284-90.
29. Greco AV, Mingrone G, Giancaterini A, et al. Insulin resistance in morbid obesity: reversal with intramyocellular fat depletion. Diabetes. 2002;51:144-151.
30. Krssak M, Falk Petersen K, Dresner A, et al. Intramyocellular lipid concentrations are correlated with insulin sensitivity in humans: a 1H NMR spectroscopy study. Diabetologia. 1999;42:113- 5.
31. Perseghin G, Scifo P, DeCobelli F, et al. Intramyocellular triglyceride content is a determinant of in vivo insulin resistance in humans: a 1H-13C nuclear magnetic resonance spectroscopy assessment in offspring of type 2 diabetic patients.Diabetes. 1999;48:1600 - 6.

ABSTRACT(IN KOREAN)

대퇴중간 저음영 근육과 저밀도 지단백 콜레스테롤 분획 크기와의 관계

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홍 정 아

목적: 신체 지방 축적은 작고 치밀한 저밀도 지단백(small dense LDL) 콜레스테롤 생성에 중요한 요인으로 특히 복부지방은 저밀도 지단백의 분자 크기와 밀접한 연관이 있음이 알려져 있다. 본 연구에서는 근육내의 지방을 나타내는 대퇴중간 저음영 근육과 다른 지단백에 비해 더 동맥경화성이며 심혈관 질환의 위험인자로 밝혀진 small dense LDL과의 관계를 알아보았다.

Methods: 만성 질환이 없는 237명의 여성을 대상으로 문진 및 신체계측, 혈액검사를 시행하고 CT로 대퇴중간 저음영 근육을 측정하였다. 대퇴중간 저음영 근육을 사분위수로 나눈뒤 심혈관위험인자와의 관련성 보기위해 ANOVA test 하였으며, 대퇴중간 저음영 근육과 피어슨 상관분석과 다중적 회귀분석을 시행하였다.

Results: 대퇴중간 저음영 근육 면적이 증가할수록 저밀도 지단백 콜레스테롤의 크기는 작아졌다(P=0.046).

Conclusion: 대퇴중간 저음영 근육은 더 동맥경화성인 small dense LDL과 독립적인 연관성이 있었으며 이는 하체 근육내의

지방과 동맥경화와의 관련성을 시사한다.

핵심되는 말 : 저밀도 지단백 콜레스테롤 분획, 대퇴중간 저음영 근육, 신체 지방 분포