

1-1-2012

The relationship between insulin resistance and carotid artery intima-media thickness in obese and morbidly obese women

GÜLÇİN CENGİZ ECEMİŞ

HAKKI KAHRAMAN

MEHMET SELİM NURAL

HALİL SERDAR ASLAN

AYŞEGÜL ATMACA

Follow this and additional works at: <https://journals.tubitak.gov.tr/medical>



Part of the [Medical Sciences Commons](#)

Recommended Citation

ECEMİŞ, GÜLÇİN CENGİZ; KAHRAMAN, HAKKI; NURAL, MEHMET SELİM; ASLAN, HALİL SERDAR; and ATMACA, AYŞEGÜL (2012) "The relationship between insulin resistance and carotid artery intima-media thickness in obese and morbidly obese women," *Turkish Journal of Medical Sciences*: Vol. 42: No. 6, Article 27. <https://doi.org/10.3906/sag-1104-43>

Available at: <https://journals.tubitak.gov.tr/medical/vol42/iss6/27>

This Article is brought to you for free and open access by TÜBİTAK Academic Journals. It has been accepted for inclusion in Turkish Journal of Medical Sciences by an authorized editor of TÜBİTAK Academic Journals. For more information, please contact academic.publications@tubitak.gov.tr.

The relationship between insulin resistance and carotid artery intima-media thickness in obese and morbidly obese women

Gülçin Cengiz ECEMİŞ¹, Hakkı KAHRAMAN¹, Mehmet Selim NURAL², Halil Serdar ASLAN²,
Ayşegül ATMACA¹

Aim: To compare insulin resistance and carotid intima-media thickness (IMT) between obese, morbidly obese, and healthy women and demonstrate whether there is a relation between these parameters, focusing mainly on morbidly obese women.

Materials and methods: Twenty-five morbidly obese women (body mass index (BMI) ≥ 40 kg/m²), 25 obese women (BMI 30–39.9 kg/m²), and 25 age-matched healthy women (BMI 18.5–24.9 kg/m²) were recruited for the study. None of the subjects had diabetes mellitus. BMI, waist-to-hip ratio, lipid profiles, fasting glucose and insulin levels, insulin resistance (by HOMA), and IMT (common carotid, internal carotid, and bifurcation measurements) were compared among the 3 groups and between obese and morbidly obese women.

Results: IMT, HOMA, triglyceride, HDL cholesterol, fasting glucose, and insulin levels were higher in obese and morbidly obese women. In the morbidly obese women, internal carotid IMT was positively correlated with fasting insulin. In the combined group of obese and morbidly obese women, internal carotid IMT was positively correlated with both fasting insulin and HOMA.

Conclusion: Increased carotid IMT is an early sign of atherosclerosis in nondiabetic obese women as well and is related to both hyperinsulinemia and insulin resistance.

Key words: Obesity, morbid obesity, carotid artery intima media thickness, insulin resistance, hyperinsulinemia

Introduction

Android obesity is the deposition of fat in the abdominal region, around the visceral organs. It leads to insulin resistance, which is associated with increased risk of diabetes mellitus (DM), dyslipidemia, hypertension, and atherosclerosis, resulting in increased morbidity and mortality rates (1). Insulin sensitivity is decreased by 30% to 40% in people who are 35% more than their ideal weight (2). Hyperinsulinemia per se is also associated with most of the risk factors of atherosclerosis and is an independent risk factor for coronary artery disease (3).

Measurement of carotid artery intima-media thickness (IMT) with high resolution B-mode ultrasonography is a valuable method for monitoring atherosclerotic changes (4). Every 0.1 mm increase in carotid artery IMT is associated with an 11% increase in the risk of acute myocardial infarction (5).

Many studies have been conducted to show the relation between insulin resistance and coronary artery disease. However, there are methodological differences among these studies regarding the patient characteristics, methods used to determine insulin resistance, drugs used, and period of follow-up.

Received: 20.04.2011 – Accepted: 06.12.2011

¹ Department of Internal Medicine, Division of Endocrinology and Metabolism, Faculty of Medicine, Ondokuz Mayıs University, Samsun - TURKEY

² Department of Radiology, Faculty of Medicine, Ondokuz Mayıs University, Samsun - TURKEY

Correspondence: Ayşegül ATMACA, Department of Internal Medicine, Division of Endocrinology and Metabolism, Faculty of Medicine, Ondokuz Mayıs University,

55139 Kurupelit, Samsun - TURKEY

E-mail: atmaca_aysegul@yahoo.com

The results of these studies also differ. Some studies demonstrate a relation between hyperinsulinemia or insulin resistance and carotid IMT, while others do not. To date, no study has been conducted to show whether there are any differences in insulin resistance and carotid IMT between obese and morbidly obese patients. The aim of this study was to compare insulin resistance, lipid parameters, blood pressure, and carotid IMT among obese, morbidly obese, and healthy control groups and to demonstrate whether there is a relation between these parameters, focusing mainly on morbidly obese patients.

Materials and methods

Twenty-five morbidly obese women (body mass index (BMI) ≥ 40 kg/m²), 25 obese women (BMI 30.0–39.9 kg/m²), and 25 healthy age-matched women as the control group (BMI 18.5–24.9 kg/m²) were enrolled in the study. Subjects with DM, other endocrine disorders, congestive heart failure, chronic renal and hepatic failure, acute or chronic infection, and cancer were excluded from the study. Subjects who were less than 18 years old, who used antihypertensive drugs, or whose systolic and diastolic blood pressures were ≥ 210 mmHg and ≥ 120 mmHg, respectively, were also excluded. Informed consent was obtained from all subjects and the study was conducted in accordance with principals of the Declaration of Helsinki.

Age (years), height (m), weight (kg), waist and hip circumferences (cm), and systolic and diastolic blood pressures (mmHg) were noted for all subjects. Waist-to-hip ratios and BMIs were calculated. Blood samples were drawn after an overnight fast of 12 h between 08.00 and 09.00 hours for fasting plasma glucose, insulin, triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. A 75-g oral glucose tolerance test was performed following a diet with ≥ 150 g/day of carbohydrates for 3 days to exclude DM. After an overnight fast, subjects were asked to drink 75 g of glucose in 200 mL water in 5 min. Blood was drawn for glucose and insulin before and 2 h after glucose loading. Insulin resistance was determined according to the Homeostasis Model Assessment (HOMA) formula (6):

$$[\text{Fasting insulin (mIU/L)} \times \text{fasting glucose (mg/dL)} \times 0.05551] / 22.5.$$

Carotid artery IMT of all subjects was measured with high resolution B-mode ultrasonography by the same radiologist. Ultrasonography was performed with real-time equipment (PowerVision 7000 SSA-380A; Toshiba Corporation, Tokyo, Japan) and a 10-MHz linear probe. The 6 sites that were measured were the right and left common carotid artery (CCA), right and left internal carotid artery (ICA), and right and left bifurcation (BCA). The measurements were carried out in regions without plaque formation. The mean of the right and left measurements was used for the analyses.

Statistical analyses were carried out with SPSS 13.0. Values were expressed as mean \pm standard deviation. $P < 0.05$ was considered statistically significant. Normality was tested by the Kolmogorov–Smirnov test. Normally distributed data were analyzed by using one-way ANOVA and differences between groups were analyzed by Tukey multiple comparisons. Nonnormally distributed data were analyzed by the Kruskal–Wallis test and differences between groups were analyzed by the Mann–Whitney U test. The Pearson correlation test was used for correlation analysis.

Results

Clinical characteristics and laboratory parameters of the groups are shown in Table 1. There was a statistically significant difference in the IMT of the CCA, ICA, and BCA, and the triglyceride, HDL cholesterol, fasting plasma glucose, and insulin levels among the 3 groups (Table 1, Figures 1a–1c). There was also a statistically significant difference in CCA, ICA, and BCA IMTs when obese and morbidly obese groups were compared separately (Table 2). Waist-to-hip ratio, systolic and diastolic blood pressures, triglyceride, total cholesterol, LDL and HDL cholesterol levels, fasting plasma glucose and insulin levels, and HOMA indexes were not statistically significant between the 2 groups (Table 2).

There was a statistically significant difference in HOMA indexes among the 3 groups ($P = 0.0001$) (Table 1). However, the difference was not statistically significant when obese and morbidly obese groups

Table 1. Clinical characteristics and laboratory parameters of the study groups.

| | Morbidly obese | Obese | Control | P-value |
|--------------------------|----------------|--------------|--------------|---------|
| Age (years) | 44.7 ± 9.8 | 44.7 ± 12.5 | 41.8 ± 11.2 | NS |
| BMI (kg/m ²) | 47.9 ± 5.6 | 34.9 ± 2.5 | 22.3 ± 1.9 | 0.0001 |
| WHR | 0.86 ± 0.06 | 0.86 ± 0.05 | 0.80 ± 0.00 | 0.0001 |
| SBP (mmHg) | 139.0 ± 20.7 | 134.0 ± 20.0 | 107.4 ± 12.2 | 0.0001 |
| DBP (mmHg) | 89.4 ± 13.0 | 86.0 ± 12.9 | 70.2 ± 11.4 | 0.0001 |
| TG (mg/dL) | 162.1 ± 79.3 | 137.9 ± 67.2 | 86.1 ± 45.5 | 0.0001 |
| TC (mg/dL) | 203.7 ± 44.6 | 205.3 ± 45.6 | 178.6 ± 47.7 | NS |
| LDL-C (mg/dL) | 125.3 ± 38.3 | 116.0 ± 41.2 | 99.7 ± 36.5 | NS |
| HDL-C (mg/dL) | 45.3 ± 13.1 | 54.3 ± 15.6 | 62.8 ± 16.9 | 0.001 |
| Fasting glucose (mg/dL) | 95.2 ± 12.7 | 95.9 ± 14.1 | 79.3 ± 8.7 | 0.0001 |
| Fasting insulin (mIU/L) | 17.2 ± 9.0 | 11.7 ± 7.0 | 5.4 ± 4.3 | 0.0001 |
| HOMA | 4.1 ± 2.3 | 2.8 ± 1.8 | 1.1 ± 1.0 | 0.0001 |
| CCA IMT (mm) | 0.7 ± 0.2 | 0.6 ± 0.2 | 0.4 ± 0.1 | 0.0001 |
| ICA IMT (mm) | 0.6 ± 0.1 | 0.5 ± 0.1 | 0.3 ± 0.1 | 0.0001 |
| BCA IMT (mm) | 0.7 ± 0.2 | 0.6 ± 0.2 | 0.5 ± 0.1 | 0.0001 |

BMI, body mass index; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; HOMA, homeostasis model assessment; CCA IMT, intima media thickness of common carotid artery; ICA IMT, intima media thickness of internal carotid artery; BCA IMT, intima media thickness of common carotid artery bifurcation.

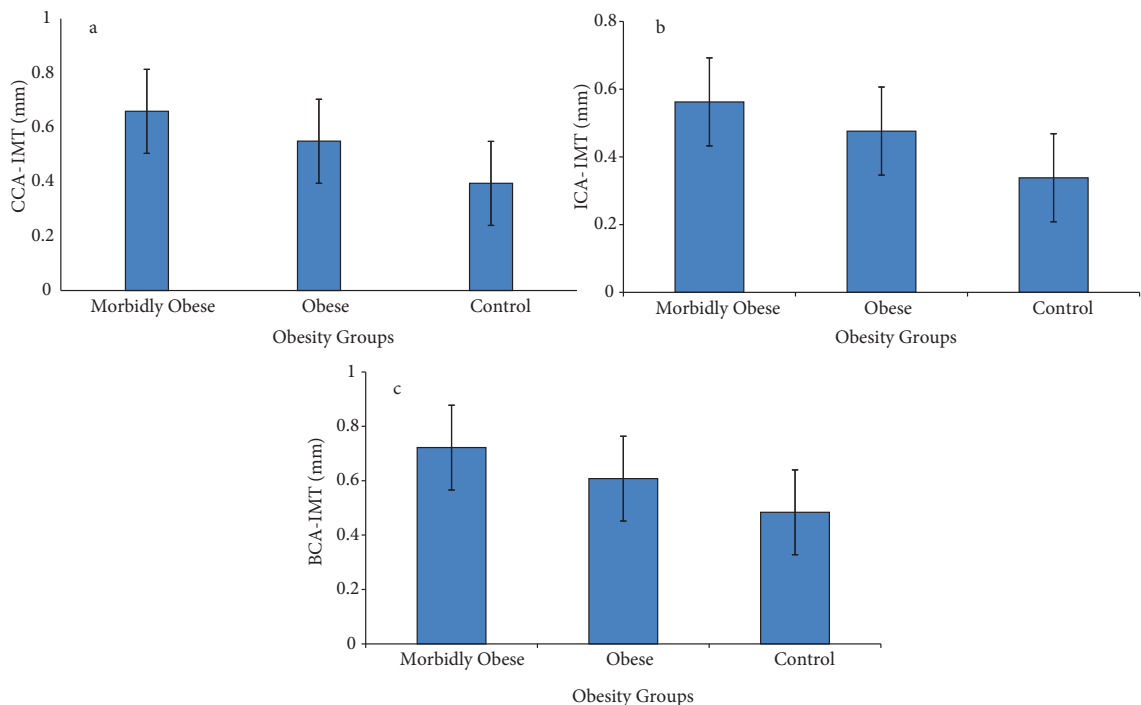


Figure 1. The mean a) CCA IMT, b) ICA IMT, and c) BCA IMT of the study groups (P = 0.0001 for all).

Table 2. Clinical characteristics and laboratory parameters of morbidly obese and obese women.

| | Morbidly obese | Obese | P-value |
|--------------------------|----------------|--------------|---------|
| Age (years) | 44.7 ± 9.8 | 44.7 ± 12.5 | NS |
| BMI (kg/m ²) | 47.9 ± 5.6 | 34.9 ± 2.5 | 0.0001 |
| WHR | 0.86 ± 0.06 | 0,86 ± 0.05 | NS |
| SBP (mmHg) | 139.0 ± 20.7 | 134.0 ± 20.0 | NS |
| DBP (mmHg) | 89.4 ± 13.1 | 86.0 ± 12.9 | NS |
| TG (mg/dL) | 162.1 ± 79.4 | 137.9 ± 67.2 | NS |
| TC (mg/dL) | 203.7 ± 44.6 | 205.3 ± 45.6 | NS |
| LDL-C (mg/dL) | 125.3 ± 38.3 | 116.0 ± 41.2 | NS |
| HDL-C (mg/dL) | 45.3 ± 13.1 | 54.3 ± 15.6 | NS |
| Fasting glucose (mg/dL) | 95.2 ± 12.7 | 95.9 ± 14.1 | NS |
| Fasting insulin (mIU/L) | 17.2 ± 9.0 | 11.7 ± 7.0 | NS |
| HOMA | 4.1 ± 2.3 | 2.8 ± 1.8 | NS |
| CCA IMT (mm) | 0.7 ± 0.2 | 0.6 ± 0.2 | 0.036 |
| ICA IMT (mm) | 0.6 ± 0.1 | 0.5 ± 0.1 | 0.028 |
| BCA IMT (mm) | 0.7 ± 0.2 | 0.6 ± 0.1 | 0.035 |

BMI, body mass index; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; HOMA, homeostasis model assessment; CCA IMT, intima media thickness of common carotid artery; ICA IMT, intima media thickness of internal carotid artery; BCA IMT, intima media thickness of common carotid artery bifurcation.

were compared separately (Table 2). In the morbidly obese group, there was no correlation between HOMA index and BMI or between HOMA index and IMT measurements. The mean ICA IMT was positively correlated with fasting insulin ($r = 0.40$, $P = 0.03$) (Figure 2). In the morbidly obese group, a negative correlation between HDL cholesterol and fasting insulin ($r = -0.6$, $P = 0.004$) and between HDL cholesterol and HOMA index ($r = -0.5$, $P = 0.007$) was also found.

When the morbidly obese and obese groups were combined (all women with BMI ≥ 30 kg/m²), the ICA IMT was positively correlated with fasting insulin ($r = 0.35$, $P = 0.01$) and HOMA index ($r = 0.30$, $P = 0.02$) (Figures 3a and 3b). In the combined group, there was also a positive correlation between BMI and ICA IMT ($r = 0.30$, $P = 0.04$) and BMI and CCA IMT ($r = 0.30$, $P = 0.04$) (Figures 4a and 4b).

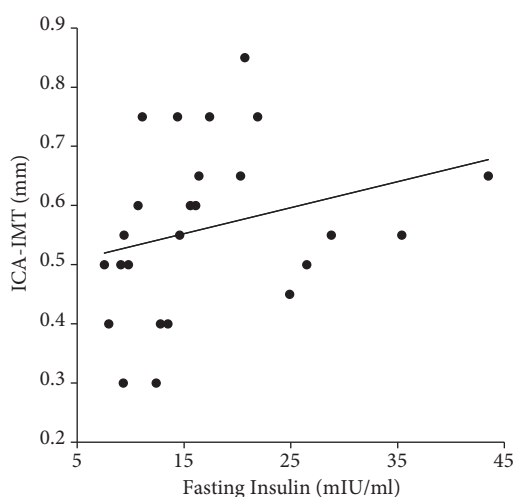


Figure 2. Correlation between ICA IMT and fasting insulin in morbidly obese women ($r = 0.40$, $P = 0.03$).

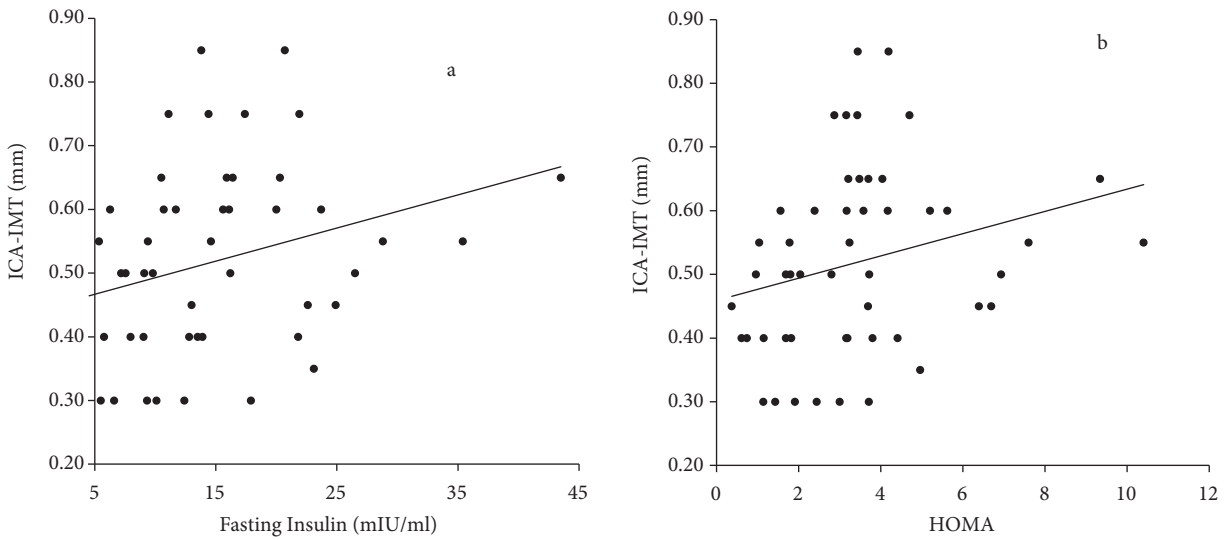


Figure 3. Correlation between a) ICA IMT and fasting insulin ($r = 0.35$, $P = 0.01$) and b) ICA IMT and HOMA index ($r = 0.30$, $P = 0.02$) in all obese women with $BMI \geq 30 \text{ kg/m}^2$.

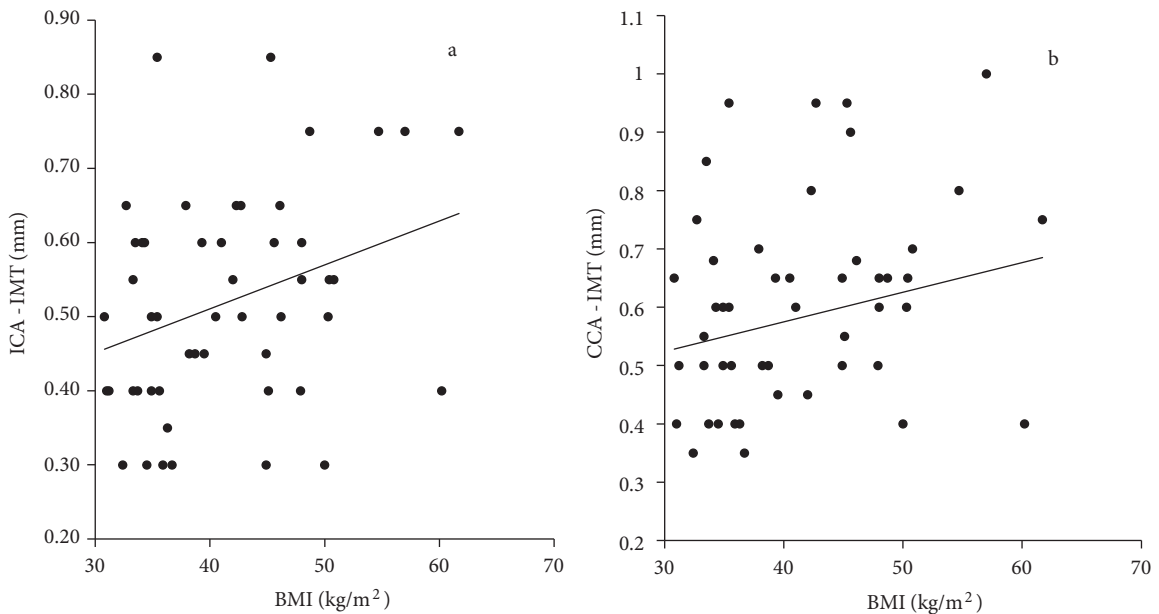


Figure 4. Correlation between a) ICA IMT and BMI ($r = 0.30$, $P = 0.04$) and b) CCA IMT and BMI ($r = 0.30$, $P = 0.04$) in all obese women with $BMI \geq 30 \text{ kg/m}^2$.

Discussion

Obesity is generally related with insulin resistance, which leads to hypertension, type 2 DM, and dyslipidemia (7). The gold standard for the evaluation of insulin resistance is the hyperinsulinemic euglycemic glucose clamp technique. However, its use is limited because it is invasive, expensive, time-consuming, and complex (8). The HOMA index is calculated with the use of fasting glucose and insulin.

It is better correlated with hepatic than peripheral insulin sensitivity (9). Sourij et al. compared the short insulin tolerance test and HOMA in 1171 overweight patients and demonstrated that HOMA is better correlated with carotid artery IMT and atherosclerosis than the short insulin tolerance test (10). Since it is easy to perform, cost-effective, and noninvasive, the HOMA index was used to evaluate insulin resistance in this study.

In this study, there was a positive correlation between fasting insulin and ICA IMT in morbidly obese women. However, there was no correlation between the HOMA index and any of the IMT measurements. To date, no study has evaluated the carotid artery IMT and its relation with insulin levels and insulin resistance in morbidly obese patients only. When obese and morbidly obese women were combined as one group, both fasting insulin levels and the HOMA index were positively correlated with ICA IMT. The reason why no correlation was found between the HOMA index and IMT measurements in morbidly obese women and a positive correlation was found when the groups were combined might be the smaller number of patients in the morbidly obese group.

Ciccione et al. could not demonstrate a correlation between fasting insulin levels and CCA IMT in obese ($\text{BMI} \geq 27 \text{ kg/m}^2$) and nonobese ($\text{BMI} < 27 \text{ kg/m}^2$) men and women (11). Likewise, De Pergola et al. found no correlation between fasting insulin levels and CCA IMT in normal weight ($\text{BMI} < 25 \text{ kg/m}^2$), overweight ($\text{BMI} 25\text{--}30 \text{ kg/m}^2$), and obese ($\text{BMI} > 30 \text{ kg/m}^2$) premenopausal women (12). However, they found a positive correlation between insulin resistance measured by insulin tolerance test and CCA IMT. They commented that this relationship was independent of other cardiovascular risk factors and insulin resistance per se accelerated the atherosclerotic process. High insulin level is generally regarded as a predictor of insulin resistance. However, fasting insulin level is an indirect and insensitive measure of insulin resistance. Therefore, according to the authors of the study, the discrepancy between the relationship of fasting insulin levels and IMT and insulin resistance and IMT is not surprising. In this study, we found that both fasting insulin levels and the HOMA index were positively correlated with ICA IMT in the combined group. Shinozaki et al. and Suzuki et al. also demonstrated a positive correlation between insulin resistance and IMT in men and women with $\text{BMI} < 25 \text{ kg/m}^2$ (13,14). In the study by Shinozaki et al., patients with vasospastic angina pectoris were included (13). In the study by Suzuki et al., patients with essential hypertension were included (14). In our study, patients with other comorbidities that could affect the results were excluded. The correlation with CCA IMT was also shown in an obese children population (15).

Not all studies show a correlation between insulin resistance and carotid artery atherosclerosis. Bonora et al. compared nondiabetic subjects with a mean BMI of 24.8 kg/m^2 with diabetic patients with a mean BMI of 29.4 kg/m^2 (3). The patient groups were not in the obesity range. They only found a positive correlation between insulin resistance and IMT in diabetic patients. In a population-based study in nondiabetic subjects, Hedblad et al. found a positive correlation between HOMA index and IMT; however, this correlation disappeared after adjustments for other confounders were made (16).

In this study, there was a statistically significant difference in carotid artery IMT measurements among the 3 groups, being greatest in the morbidly obese group. In the combined morbidly obese and obese group, BMI was positively correlated with CCA and ICA IMT. This result shows that excess body fat is related to arterial wall thickness and atherosclerosis is accelerated in obesity. Carotid artery IMT is used as a marker for end organ damage because increased IMT is an early change in the atherosclerotic process. In a study by Salonen and Salonen, CCA IMT was positively correlated with the risk of coronary heart disease (17). The results of our study are in concordance with other studies (11,18–20).

Measurement of carotid artery IMT by B-mode ultrasonography is recommended for risk assessment by the American Heart Association (21). In most of the studies, different regions were used, but the results may differ according to the region selected. Focal atherosclerotic plaques are found to be more prevalent in the ICA than the CCA. Likewise, ICA IMT is much more correlated with coronary artery disease and myocardial risk factors than CCA IMT (22). In this study, bilateral ICA, CCA, and BCA measurements were done and the mean values of the right and left were calculated. ICA IMT, which is more valuable than CCA IMT as discussed above, was found to be better correlated with parameters such as fasting insulin and HOMA indexes.

When lipid profiles were compared, only triglyceride and HDL cholesterol differed significantly among the 3 groups. When the combined group of obese and morbidly obese women was compared to the control group, all of the lipid parameters differed significantly. Similar results were shown in other

studies (23–26). When morbidly obese and obese groups were compared separately, none of the lipid parameters differed significantly. These results were similar to the results of another study in which the metabolic profile of morbidly obese (BMI ≥ 40 mg/m²) women was not deteriorated as expected when compared to moderately obese (BMI 30–40 kg/m²) women (27). Therefore, it can be assumed that the degree of obesity may not be directly correlated with the deterioration of the lipid profile. In the morbidly obese group, HDL cholesterol, but no other lipid parameters, was negatively correlated with fasting insulin and the HOMA index. Hyperinsulinemia is shown to be related to increases in triglycerides and

decreases in HDL cholesterol rather than any changes in total or LDL cholesterol (28). Defects in insulin signaling may result in proatherogenic lipid profiles in peripheral tissues such as adipose tissue (29).

In conclusion, this study shows the relation between BMI, hyperinsulinemia, insulin resistance, and carotid artery IMT. The results confirm that obesity is related with carotid artery IMT and accelerates atherosclerosis. Although there are studies showing this relationship, the morbidly obese group was analyzed separately in this study. Studies with more patients will further clarify the results of this study.

References

- Caro JF, Dohm LG, Pories WJ, Sinha MK. Cellular alteration in liver, skeletal muscle, adipose tissue responsible for insulin resistance in obesity and type II diabetes. *Diabetes Metab Rev* 1989; 5: 665–89.
- DeFronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; 14: 173–94.
- Bonora E, Tessari R, Micciolo R, Zenere M, Targher G, Padovani R et al. Intimal-medial thickness of the carotid artery in non-diabetic and NIDDM patients. Relationship with insulin resistance. *Diabetes Care* 1997; 20: 627–31.
- Lonn E. Carotid artery intima-media thickness -- a new noninvasive gold standard for assessing the anatomic extent of atherosclerosis and cardiovascular risk? *Clin Invest Med* 1999; 22: 158–60.
- Boden G, Shulman GI. Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and β -cell dysfunction. *Eur J Clin Invest* 2002; 32: 14–23.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28: 412–9.
- Thomas GN, Ho SY, Lam KS, Janus ED, Hedley AJ, Lam TH. Impact of obesity and body fat distribution on cardiovascular risk factors in Hong Kong Chinese. *Obes Res* 2004; 12: 1805–13.
- Garrapa GG, Canibus P, Gatti C, Santangelo M, Frezza F, Feliciotti F et al. Changes in body composition and insulin sensitivity in severely obese subjects after laparoscopic adjustable silicone gastric banding (LASGB). *Med Sci Monit* 2005; 11: 522–8.
- Bonora E, Targher G, Alberiche M, Bonadonna RC, Saggiani F, Zenere MB et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. *Diabetes Care* 2000; 23: 57–63.
- Sourij H, Schmoelzer I, Dittrich P, Paulweber B, Iglseider B, Wascher TC. Insulin resistance as a risk factor for carotid atherosclerosis: a comparison of the Homeostasis Model Assessment and the short insulin tolerance test. *Stroke* 2008; 39: 1349–51.
- Ciccione M, Maiorano A, De Pergola G, Minenna A, Giorgino R, Rizzon P. Microcirculatory damage of common carotid artery wall in obese and nonobese subjects. *Clin Hemorheol Microcirc* 1999; 21: 365–74.
- De Pergola G, Ciccione M, Pannacciulli N, Modugno M, Sciaraffia M, Minenna A et al. Lower insulin sensitivity as an independent risk factor for carotid wall thickening in normotensive, non-diabetic, non-smoking normal weight and obese premenopausal women. *Int J Obes Related Metab Disord* 2000; 24: 825–9.
- Shinozaki K, Hattori Y, Suzuki M, Hara Y, Kanazawa A, Takaki H et al. Insulin resistance as an independent risk factor for carotid artery wall intima media thickening in vasospastic angina. *Arterioscler Thromb Vasc Biol* 1997; 17: 3302–10.
- Suzuki M, Shinozaki K, Kanazawa A, Hara Y, Hattori Y, Tsushima M et al. Insulin resistance as an independent risk factor for carotid wall thickening. *Hypertension* 1996; 28: 593–8.
- Atabek ME, Pirgon O, Kivrak AS. Evidence for association between insulin resistance and premature carotid atherosclerosis in childhood obesity. *Pediatr Res* 2007; 61: 345–9.

16. Hedblad B, Nilsson P, Janzon L, Berglund G. Relation between insulin resistance and carotid intima-media thickness and stenosis in non-diabetic subjects. Results from a cross-sectional study in Malmö, Sweden. *Diabet Med* 2000; 17: 299–307.
17. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. *Arterioscler Thromb* 1991; 11: 1245–9.
18. De Michele M, Panico S, Iannuzzi A, Celentano E, Ciardullo AV, Galasso R et al. Association of obesity and central fat distribution with carotid artery wall thickening in middle-aged women. *Stroke* 2002; 33: 2923–8.
19. Oflaz H, Ozbey N, Mantar F, Genchellac H, Mercanoglu F, Sencer E et al. Determination of endothelial function and early atherosclerotic changes in healthy obese women. *Diabetes Nutr Metab* 2003; 16: 176–81.
20. Iannuzzi A, Licenziati MR, Acampora C, Salvatore V, Auriemma L, Romano ML et al. Increased carotid intima-media thickness and stiffness in obese children. *Diabetes Care* 2004; 27: 2506–8.
21. O'Leary DH, Polak JF. Intima-media thickness: a tool for atherosclerosis imaging and event prediction. *Am J Cardiol* 2002; 90: 18–21.
22. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med* 1999; 340: 14–22.
23. Barakat HA, Mooney N, O'Brien K, Long S, Khazani PG, Pories W et al. Coronary heart disease risk factors in morbidly obese women with normal glucose tolerance. *Diabetes Care* 1993; 16: 144–9.
24. Hu D, Hannah J, Gray RS, Jablonski KA, Henderson JA, Robbins DC et al. Effects of obesity and body fat distribution on lipids and lipoproteins in nondiabetic American Indians: The Strong Heart Study. *Obes Res* 2000; 8: 411–21.
25. Dixon JB, O'Brien P. A disparity between conventional lipid and insulin resistance markers at body mass index levels greater than 34 kg/m². *Int J Obes Relat Metab Disord* 2001; 25: 793–7.
26. Njelekela MA, Negishi H, Nara Y, Sato T, Tomohiro M, Kuga S et al. Obesity and lipid profiles in middle aged men and women in Tanzania. *East Afr Med J* 2001; 79: 58–64.
27. Drapeau V, Lemieux I, Richard D, Bergeron J, Tremblay A, Biron S et al. Metabolic profile in severely obese women is less deteriorated than expected when compared to moderately obese women. *Obes Surg* 2006; 16: 501–9.
28. Stout RW. Insulin and atheroma. 20-yr perspective. *Diabetes Care* 1990; 13: 631–54.
29. Semenkovich CF. Insulin resistance and atherosclerosis. *J Clin Invest* 2006; 116: 1813–22.