Lipid discordance and carotid plaque in obese patients in primary prevention

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KEYWORDS
Obesity; Lipid discordance; Carotid atherosclerotic plaque

Abstract
Introduction: Obese patients with lipid discordance (non-HDL cholesterol levels 30 mg/dl above the LDL-c value) may have a greater prevalence of carotid atherosclerotic plaque (CAP). Our study objectives were: (1) To assess the prevalence of lipid discordance in a primary prevention population of obese patients; (2) To investigate the association between lipid discordance and presence of CAP.

Methods: Obese subjects aged >18 years (BMI ≥ 30 kg/m²) with no cardiovascular disease, diabetes, or lipid-lowering treatment from six cardiology centers were included. Lipid discordance was defined when, regardless of the LDL-c level, the non-HDL cholesterol value exceeded the LDL-c value by 30 mg/dl. Presence of CAP was identified by ultrasonography. Univariate and multivariate analyses were performed to explore the association between lipid discordance and presence of CAP.

Results: The study sample consisted of 325 obese patients (57.2% men; mean age, 52.3 years). Prevalence of lipid discordance was 57.9%. CAP was found in 38.6% of patients, but the proportion was higher in subjects with lipid discordance as compared to those without this lipid pattern (44.4% vs. 30.7%, p = 0.01). In both the univariate (OR: 1.80; 95% CI: 1.14–2.87; p = 0.01) and the multivariate analysis (OR: 2.07; 95% CI: 1.22–3.54; p = 0.007), presence of lipid discordance was associated to an increased probability of CAP.

Conclusion: In these obese patients, lipid discordance was associated to greater prevalence of CAP. Evaluation of obese patients with this strategy could help identify subjects with higher residual cardiovascular risk.

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Introducción

La obesidad es un problema de salud global que ha aumentado significativamente en la mayoría de los países. La obesidad no solo es un problema de salud física, sino que también puede llevar a complicaciones graves de la salud mental. Además, la obesidad aumenta el riesgo de desarrollar enfermedades crónicas como la diabetes tipo 2, enfermedades cardíacas y algunos tipos de cáncer. Estos problemas representan un gran desafío para la salud pública a nivel mundial. En este contexto, se ha identificado la necesidad de desarrollar estrategias efectivas para prevenir y controlar la obesidad, así como para analizar los factores que contribuyen a su desarrollo.

Métodos:

Se utilizó un estudio prospectivo en un grupo de pacientes con obesidad. Se realizó un análisis descriptivo de los datos obtenidos. Se definieron los criterios diagnósticos para la obesidad y se evaluaron los factores asociados. Se llevó a cabo una revisión exhaustiva de la literatura disponible para comparar los resultados obtenidos con los hallados en otros estudios. Se utilizaron diferentes técnicas estadísticas como análisis de regresión lineal para analizar la relación entre los factores de riesgo y la obesidad.

Resultados:

Se incluyeron 325 pacientes con obesidad, los cuales se clasificaron en dos grupos: uno con obesidad abdominal y otro con obesidad generalizada. Se observó una alta prevalencia de obesidad abdominal en comparación con la obesidad generalizada, lo que sugiere que la obesidad abdominal es un factor de riesgo importante para la salud. Se encontró una asociación significativa entre la obesidad y la presión arterial, el colesterol total, el colesterol HDL y el triglicéridos. Se observó que los pacientes con obesidad abdominal tenían un mayor riesgo de desarrollar enfermedades cardiovasculares en comparación con aquellos con obesidad generalizada.

Conclusiones:

La obesidad es un problema de salud pública importante que requiere de estrategias eficaces para su prevención y control. Los resultados de este estudio muestran la importancia de identificar y tratar la obesidad abdominal como un factor de riesgo independiente para la salud. Se recomienda la implementación de programas de promoción de la salud y manejo del peso en la población general, así como la realización de estudios adicionales para profundizar en el conocimiento de esta problemática.
Lipid thickness egorical 33.6 standards, of tern test lumen, 180.1 triglycerides by those recent level cholesterol taken dimensional percentages. The Lipid Independently Statistical We likewise treatment ± < defined in prevalence (males females population. The discordance'' was observed greater BMI (6.1 ± 1.2 vs. 2.6 ± 1.2; p < 0.001). Table 3 describes the values of the lipid variables according to concordant or discordant lipid patterns. A good correlation was found between LDL-cholesterol and non-HDL-cholesterol (r = 0.855). The distribution of LDL-cholesterol and non-HDL-cholesterol in the global population, together with the lipid discordance or concordance categories, are shown in Fig. 1. The proportion of patients with lipid discordance was significantly greater in the upper BMI tertile (mean 38.2 ± 2.9 kg/m²) than in the lower tertile (mean 30.9 ± 0.6 kg/m²), in both the global population and among the males. A statistically non-significant trend was observed in females (Fig. 2).

Carotid atherosclerotic plaque was identified in 38.6% of the patients (males 37.8%, females 39.6%). This proportion was greater among the individuals with lipid discordance than in those without it (44.4% vs. 30.7%; p = 0.01).

In the univariate analysis, the presence of lipid discordance was associated with an average 80% greater probability of CAP (OR: 1.80; 95%CI: 1.14–2.87; p = 0.01). In the multivariate analysis (adjusted for age, gender, the BMI and the Framingham score), obese patients with lipid discordance doubled the probability of having CAP in the ultrasound study compared with the individuals without CAP (OR: 2.07; 95%CI: 1.22–3.54; p = 0.007).

**Results**

A total of 325 obese patients were included in the study. Of these, 57.2% were males, and the mean age was 52.3 years. The concentrations (mean ± SD) corresponding to total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides were 217.6 ± 39.5, 138.0 ± 35, 42.9 ± 10.8 and 180.1 ± 92.1 mg/dl, respectively. Table 1 describes the characteristics of the study population.

Lipid discordance was observed in 57.9% of the global sample (males 59.1%, females 56.2%). The patients with lipid discordance had a greater BMI (34.4 ± 3.6 kg/m² vs. 33.6 ± 3.4 kg/m²; p = 0.03) and a higher Framingham score (9.3 ± 7.3% vs. 7.3 ± 7.0%; p = 0.01) than the subjects without lipid discordance. There were no significant differences in the other non-lipidic variables analyzed (Table 2).

The HDL-cholesterol/triglyceride ratio was significantly higher in the patients with lipid discordance than in those without such a lipid profile (6.1 ± 1.2 vs. 2.6 ± 1.2; p < 0.001). Table 3 describes the values of the lipid variables according to concordant or discordant lipid patterns.

**Table 1** Characteristics of the study population (No. = 325).

<table>
<thead>
<tr>
<th>Continuous variables, mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>52.3 (11.2)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>2176 (39.5)</td>
</tr>
<tr>
<td>LDL-cholesterol, mg/dl</td>
<td>1380 (35.0)</td>
</tr>
<tr>
<td>HDL-cholesterol, mg/dl</td>
<td>42.9 (10.8)</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>1801 (92.1)</td>
</tr>
<tr>
<td>Non-HDL-cholesterol, mg/dl</td>
<td>1742 (39.8)</td>
</tr>
<tr>
<td>Calculated remnant cholesterol, mg/dl</td>
<td>36.4 (20.6)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>34.1 (3.5)</td>
</tr>
<tr>
<td>Framingham score</td>
<td>8.4 (7.2)</td>
</tr>
<tr>
<td>ACC/AHA 2013 score</td>
<td>8.9 (7.8)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>1335 (13.6)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>83.2 (10.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Categorical variables, %</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>57.2</td>
</tr>
<tr>
<td>Active smoking</td>
<td>24.2</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>57.9</td>
</tr>
<tr>
<td>Carotid plaque</td>
<td>38.6</td>
</tr>
</tbody>
</table>

**Discussion**

The prevalence of obesity has doubled in the last 35 years in many parts of the world. Two-thirds of all deaths related to obesity are attributable to cardiovascular disease.14
In 2013, Likewise, p < 0.001 atherosclerotic cholesterol associated to anance cholesterol non-HDL-cholesterol Total Variable, Table Age, Continuous Table Total triglyceride/HDL-cholesterol Non-HDL LDL-cholesterol, Categorical Diastolic Systolic Body Mass index, kg/m² 42 to 0.0 76 42 148 1371 (13.4) 8.2 (7.8) 1331 (13.9) 81.9 (10.0) 10.5 0.76 0.08 0.60 0.58 0.05 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001

The present study shows the presence of lipid discordance in obese patients in the context of primary prevention to be associated with an increased probability of CAP.

Carotid atherosclerotic plaque is a surrogate of cardiovascular disease, and its presence is associated with all the cardiovascular risk factors. The plasma total cholesterol and triglyceride concentrations are independently associated with the presence of CAP. Likewise, non-HDL-cholesterol and HDL-cholesterol are related to an increased atherosclerotic "burden". Megías-Rangil et al. showed dyslipidemia to be the main variable associated with carotid intima-media thickening in a group of patients with morbid obesity.

The analysis of discordance is a technique in which biologically related variables are explored according to groups exhibiting concordance or discordance between their relative distributions. In our study "lipid discordance" has been defined on an arbitrary but original basis. The lipid profile was classified as discordant for each patient when the non-HDL-cholesterol concentration exceeded the LDL-cholesterol level by 30 mg/dl. The clinical value of this analysis is therefore more closely related to the number of atherogenic particles than to the total cholesterol mass. In

![Graph](https://via.placeholder.com/150)

**Figure 1** Correlation between LDL-cholesterol and non-HDL-cholesterol in the study population. The individuals with non-HDL-cholesterol levels 30 mg/dl above the LDL-cholesterol levels were regarded as discordant.

![Bar Chart](https://via.placeholder.com/150)

**Figure 2** Proportion of obese patients with lipid discordance in relation to the body mass index (tertiles).
a group of primary prevention patients, our group previously demonstrated the association between lipid discordance and remnant cholesterol and the presence of CAP.26 In the present study we specifically examined a group of obese patients, excluding individuals with diabetes and patients receiving lipid-lowering treatment.

Lipid discordance was documented in 57.9% of the subjects. The idea that not all obese individuals present metabolic changes—including atherogenic dyslipidemia—is not new. Up to one-third of the studied obese subjects do not show the metabolic changes commonly seen in obese individuals.21 The term “healthy obese” is used in reference to these subjects and to distinguish them from the larger and more common population of obese individuals, although its true prognostic value is unclear.

Our results indicate that lipid discordance is more prevalent among individuals with higher BMI values. The novel and simplified form of identifying the atherogenic pattern of dyslipidemia in our study coincides with previous studies associating different lipid markers (apolipoprotein B, non-HDL-cholesterol, small and dense particles) to increased body weight.4

Insulin resistance is frequently seen in obese individuals and is characterized by a decrease in insulin biological function, a high plasma concentration of this hormone being needed to maintain carbohydrate, protein and lipid metabolism. The triglyceride/HDL-cholesterol ratio is regarded as a surrogate marker of insulin resistance.22 23 In our study, the triglyceride/HDL-cholesterol ratio was significantly higher in the patients with lipid discordance, thus suggesting a greater presence of insulin resistance in such individuals.

Our data indicate a greater prevalence of CAP in obese subjects with lipid discordance. This association persisted after adjusting for other potential confounding variables. These findings underscore the importance of measuring non-HDL-cholesterol beyond the LDL-cholesterol value, especially in certain populations such as obese individuals. In routine practice, many patients at high cardiovascular risk show a persistent atherogenic dyslipidemic profile despite having reached the recommended LDL-cholesterol target.24 This is clinically relevant, since failure to detect these patients implies that no action will be taken to correct the residual cardiovascular risk.

Our study has some limitations. Firstly, the study design did not allow us to rule out possible bias (mainly selection bias). The obese individuals visiting cardiovascular prevention clinics were not necessarily representative of the general population. Secondly, the waist circumference could not be documented in most of the patients; as a result, the presence of metabolic syndrome according to the classical definition could not be analyzed. On the other hand, we used the Friedewald formula to calculate LDL-cholesterol in our study. This calculation has limits when the triglyceride concentration exceeds 400 mg/dL. However, only 3% of the obese subjects in our population showed triglyceride levels above this threshold. Another limitation is the fact that while the classical risk factors (age, gender, arterial hypertension, dyslipidemia, smoking) were taken into consideration in our study, other risk factors were left out of the analysis. Lastly, the triglyceride/HDL-cholesterol ratio was used as an insulin resistance marker, and insulinemia determinations were not available in all cases.

In conclusion, the prevalence of lipid discordance in our population of obese patients was considerable. This simple way to estimate atherogenic dyslipidemia was associated with an increased prevalence of CAP. Since the detection of CAP implies increased cardiovascular risk, the characterization of obese patients from this perspective could allow us to identify obese subjects with a greater residual cardiovascular risk.

Conflicts of interest

None.

References


