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ORIGINAL ARTICLE

The impact of obesity in the cardiac lipidomic and its consequences in the cardiac damage observed in obese rats

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KEYWORDS
Lipid profiling;
Obesity;
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Abstract
Aims: To explore the impact of obesity on the cardiac lipid profile in rats with diet-induced obesity, as well as to evaluate whether or not the specific changes in lipid species are associated with cardiac fibrosis.
Methods: Male Wistar rats were fed either a high-fat diet (HFD, 35% fat) or standard diet (3.5% fat) for 6 weeks. Cardiac lipids were analyzed using by liquid chromatography-tandem mass spectrometry.
Results: HFD rats showed cardiac fibrosis and enhanced levels of cardiac superoxide anion ($O_2^{\bullet}$), HOMA index, adiposity, and plasma leptin, as well as a reduction in those of cardiac glucose transporter (GLUT 4), compared with control animals. Cardiac lipid profile analysis showed a significant increase in triglycerides, especially those enriched with palmitic, stearic, and arachidonic acid. An increase in levels of diacylglycerol (DAG) was also observed. No changes in cardiac levels of diacyl phosphatidylcholine, or even a reduction in total levels of diacyl phosphatidylethanolamine, diacyl phosphatidylinositol, and sphingomyelins (SM) was observed in HFD, as compared with control animals. After adjustment for other variables (oxidative stress,

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HOMA, cardiac hypertrophy), total levels of DAG were independent predictors of cardiac fibrosis while the levels of total SM were independent predictors of the cardiac levels of GLUT 4.
Conclusions: These data suggest that obesity has a significant impact on cardiac lipid composition, although it does not modulate the different species in a similar manner. Nonetheless, these changes are likely to participate in the cardiac damage in the context of obesity, since total DAG levels can facilitate the development of cardiac fibrosis, and SM levels predict GLUT4 levels.

PALABRAS CLAVE
Lipidómica;
Obesidad;
Remodelado cardiaco;
Fibrosis

El impacto de la obesidad sobre el lipidoma cardiaco y sus consecuencias en el daño cardiaco en ratas obesas

Resumen
Objetivos: Explorar el impacto de la obesidad sobre el perfil lipídico cardiaco en ratas con obesidad inducida por dieta. Se evaluó, además, si estos cambios se asocian con fibrosis cardiaca.
Métodos: Ratas macho Wistar fueron alimentadas con una dieta con alto contenido en grasa (HFD; 35% grasa) o con una dieta estándar (3,5% grasa) durante 6 semanas. El análisis del lipidoma cardiaco se realizó mediante cromatografía líquida en tándem con espectrofotometría de masas.
Resultados: Las ratas HFD presentaron fibrosis cardiaca, estrés oxidativo y un aumento en el índice HOMA, adiposidad y los niveles circulantes de leptina así como una reducción en los niveles cardiacos del transportador de glucosa (GLUT 4) en comparación con las ratas controles. El análisis del lipidoma cardiaco mostró un aumento de los niveles de triglicéridos especialmente los que contenían ácido palmítico, esteárico o araquidónico, un incremento en los de diacilglicerol (DAG) aunque no cambios en los de diacilfosfatidilcolina y una reducción en los de diacilfosofatidiletanolamina, diacilfosfatidilinositol o de esfingomielinas (SM) en las ratas HFD en comparación con las control. Después del ajuste por otras variables (estrés oxidativo, hipertrofia cardiaca, índice HOMA), los niveles de DAG fueron predictores independientes de fibrosis cardiaca mientras que los de SM fueron de los de niveles de GLUT4.
Conclusiones: La obesidad ejerce un impacto importante sobre el lipidoma cardiaco. Estos cambios parecen participar en el daño cardiaco en el contexto de la obesidad ya que los niveles de DAG podrían facilitar el desarrollo de fibrosis miocárdica y los de SM los de GLUT 4.

Introduction

Obesity has become a relevant health problem that is reaching epidemic proportions worldwide.[1] Obese individuals show a higher risk of cardiovascular morbidity and mortality, which has been explained through chronic low-grade inflammation, increased oxidative stress and the metabolic alterations associated with obesity which can affect cardiac function.[2] These conditions are linked to excess lipid accumulation not only in adipose tissue but also in non-adipose tissues, including the heart, which occurs when the storage capacity of adipocytes is exceeded.[3]

Lipids are important regulators of cardiac function, not only as the main energy substrate for cardiac mitochondrial oxidative metabolism but also by their role in membrane phospholipid remodeling, their activity as signaling molecules and ligands for nuclear receptors. However, increased myocardial lipid accumulation elicits an imbalance between cardiomyocyte fatty acid uptake and fatty acid oxidation,[4] which can facilitate the accumulation of cardiotoxic metabolites that can exert deleterious effects on the myocardium.[5] Clinical studies with proton magnetic resonance spectroscopy have demonstrated that increased intramyocardial triglyceride (TG) accumulation occurs before cardiac dysfunction in patients with type 2 diabetes mellitus and correlates with body mass index.[6,7] These data supporting a link between cardiac lipid accumulation and myocardial dysfunction. Experimental studies[8–11] have shown that the accumulation of some lipid species, including diacylglycerol (DAG), lyso phospholipids, acyl carnitines, ceramides and TGs, can affect cardiomyocyte function and lead to cardiac dysfunction. However, the potential mechanisms that link the lipid accumulation with the functional alterations are not well established.

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