Correlation between coronary calcium score, hepatic steatosis and metabolic syndrome

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Abstract: Objectives. *To demonstrate the correlation between the presence or absence of established coronary disease (as measured by the Agatston index) and hepatic steatosis visualized in liver segments when calculating calcium score.* Material and Methods. *Retrospective study that included 229 patients with risk factors for coronary disease who underwent multislice computed tomography of coronary arteries or calcium score. We evaluated the presence of atherosclerotic disease in coronary arteries and thoracic aorta and liver attenuation in visualized liver segments. Statistical analysis included linear regression models, association studies of multiple variables and CART model.* Results. *229 patients, 78% male and 22% female, average age 56 years. It showed statistically significant association between higher levels of calcium score and lower hepatic attenuation in older patients and males. We were able to define two types of patients with high calcium score, a group with hypertension-hepatic steatosis and another group with hypertension and type 2 diabetes; patients that were only obese did not have higher levels of calcium score.* Conclusions. *A relationship exists between calcified atheromatous and hepatic steatosis. Patients with hepatic steatosis as part of a metabolic syndrome are at increased risk of atherosclerosis. It may be useful to incorporate the assessment of hepatic steatosis in cardiovascular risk stratification.*
Keywords: *Atheromatosis, Calcium score, Hepatic steatosis, Metabolic syndrome.*

Resumen: Objetivos. *Demostrar la correlación que existe entre presencia o no de enfermedad coronaria establecida (medida a través del índice de Agatston) y esteatosis hepática en los segmentos visualizados del hígado al momento de realizar el score de calcio.* Material y Métodos. *Estudio retrospectivo que incluyó 229 pacientes con factores de riesgo para enfermedad coronaria a los que se les realizó tomografía computada multicorte de arterias coronarias o score de calcio. Se evaluó la presencia de enfermedad ateromatosa en arterias coronarias y aorta torácica y atenuación hepática en los segmentos visualizados del hígado. El análisis estadístico incluyó modelos de regresión lineal, estudio por asociación de múltiples variables y modelo CART.* Resultados. *229 pacientes, 78% de sexo masculino y 22% femenino, con edad promedio 56 años. Se demostró asociación estadísticamente significativa entre mayor nivel de score de calcio y menor atenuación hepática, en pacientes de mayor edad y sexo masculino. Se logró definir dos tipos de pacientes con score de calcio elevado, un grupo con hipertensión arterial-esteatosis hepática y otro grupo con hipertensión arterial y diabetes tipo 2; los pacientes solamente obesos no tenían mayores niveles de score de calcio.* Conclusiones. *Existe asociación entre ateromatosis calcificada y esteatosis hepática. Los pacientes con esteatosis hepática como parte de un síndrome metabólico, tienen mayor riesgo de ateroesclerosis. Puede ser útil incorporar la evaluación de esteatosis hepática en la estratificación de riesgo cardiovascular.*
Palabras clave: *Ateromatosis, Esteatosis, Hepática, Score de calcio, Síndrome metabólico.*

Introduction

Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum of pathological conditions, including simple steatosis, non-alcoholic steatohepatitis (NASH) and cirrhosis. This condition has reached epidemic proportions and is the most common cause of chronic liver disease[1].

In western countries it is estimated that approxima-

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tely 20-30% of adults in the general population have NAFLD and its prevalence increases from 70-90% among the obese or diabetics; these patients also have increased risk of developing cirrhosis[4].

The prevalence of NAFLD is expected to increase due to dietary habits and an increasingly sedentary lifestyle. Liver biopsy is considered the gold standard for the diagnosis of NAFLD, but it is invasive and can cause complications such as bleeding. Multislice computed tomography (MSCT) can be used to diagnose fatty liver, by demonstrating low attenuation in the hepatic parenchyma (82% sensitivity and 100% specificity)[2].

Hepatic steatosis (fatty liver) is closely related to various metabolic disorders, such as insulin resistance and it has been proposed as the unifying factor of metabolic disorders.

Coronary artery disease (CAD) is also related to several metabolic disorders, increasing concern that patients with NAFLD may also have an increased risk of coronary heart disease.

In cardiological practice MSCT is a noninvasive method to diagnose coronary artery disease in patients with mild or moderate cardiovascular risk factors[3].

Since fatty liver patients are at a high risk of developing diabetes and cardiovascular diseases[4], with this paper we aim to demonstrate the correlation between the presence or absence of established coronary disease (measured using the Agatston index) and hepatic steatosis in liver segments visualized when calculating calcium score[5].

Material and methods

Retrospective study that included 229 patients with risk factors for coronary heart disease, on whom were performed coronary artery MSCT or calcium score in the Department of Computed Tomography and Magnetic Resonance at the Clinica Alemana in Santiago between october 2009 and october 2010. Patients with coronary by-pass were excluded.

All examinations were performed on a 128 channel multidetector CT scanner, with prospective acquisition, ECG-triggered, without use of IV contrast medium, or prior to the use of this in the case of coronary artery MSCT (Figure 1a-c). The examinations were reviewed by two radiology specialists in cardiothoracic imaging.
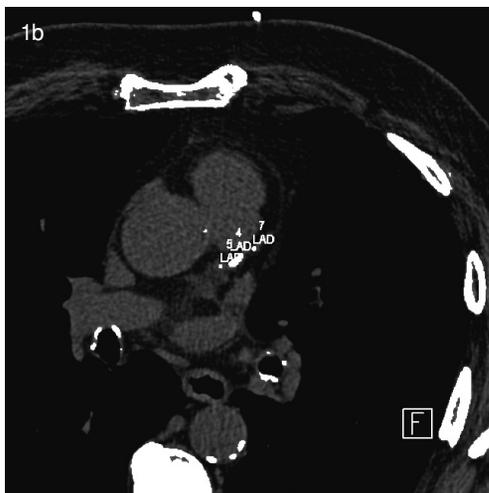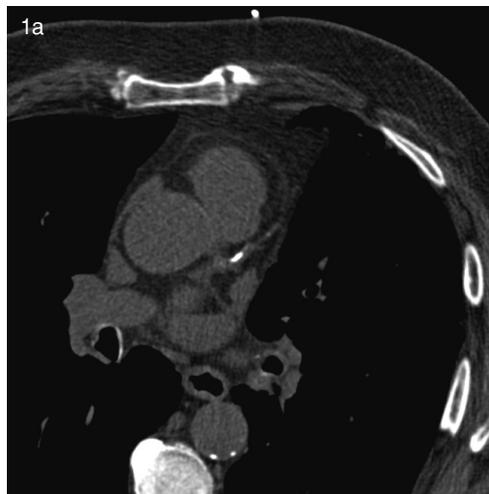
1c	Umbral = 130 HU (102.7 mg/cm³ CaHA)			
Arteria	Número de lesiones (1)	Volumen [mm³] (3)	Masa equiv. [mg CaHA] (4)	Cuantificación del calcio (2)
LM	0	0.0	0.00	0.0
LAD	8	82.3	21.87	101.8
CX	3	156.6	45.97	198.9
RCA	3	11.5	2.12	12.4
Total	14	250.3	69.96	313.1

(1) Lesión basada en volumen
(2) Equivalente Agatston Score
(3) Volumen interpolado isotrópico
(4) Factor de calibración: 0.790

Figure 1a-c. *Defining Calcium score using MSCT. The semi-automatic software indicated those pixels above the 130 HU threshold (Figure 1a, 1b), which are manually assigned to one of the coronary branches, producing a final calcium quantification value (Figure 1c).*

Patients were classified according to the presence of calcified and non-calcified atheromatous disease in coronary arteries and thoracic aorta.

Attenuation of hepatic parenchymal was measured in the visualized liver segments at the moment of calculating calcium score in Hounsfield Units (HU); this was done by applying a ROI of at least 5 cm^2 over a segment of the left hepatic lobule (Figure 2).

Figure 2. *Measurement of attenuation of hepatic parenchymal in the visualized liver segments at the moment of calculating calcium score in Hounsfield units (HU).*

The electronic medical records of the 225 selected patients were reviewed obtaining the following data: gender, age, presence of arterial hypertension (HTN), type 2 diabetes mellitus (DM), dyslipidemia, obesity and NAFLD. We excluded 4 patients who had no entries on the clinical records.

For the statistical analysis, linear regression models, study by association of multiple variables and CART model were used. The statistics program STATAv10.1 (STATA Statistical Software: Release 10. College Station, TX: StataCorp LP) was used. $p < 0.05$ as statistically significant differences were considered.

Table I. Patients characteristics

Patients	221	
Age (years)	56 (DS: 11)	
Men	172	77,8%
Women	49	22,2%
Diabetic	21	9,50%
Hypertension	90	40,72%
Dyslipidemia	139	62,90%

Results

The study population consisted of 221 patients, 172 men (78%) and 49 women (22%) with an average age of 56 years (SD ± 11). Of these, 9.5% were diabetics, 40.72 % had hypertension, and 62.9% dyslipidemia (Table I).

It was found through univariate and multivariate analysis that there are no significant differences in the distribution of hepatic attenuation values and calcium score values, evaluated by gender.

There does exist a statistically significant association between higher calcium score values with lower liver attenuation values ($p = 0.04$), older age ($p < 0.001$) and male gender ($p = 0.005$) (Figure 3).

There is not a higher association of non-calcified atheroma in relation to steatosis (neither as a continuous variable nor as a categorical). However, a statistically significant association is demonstrated between the presence of calcified atheroma and hepatic steatosis.

Applying a linear regression model, we studied the relationship between calcium score values (as a dependent variable) and the attenuation values of the hepatic parenchyma (HU), patients age, gender, hypertension, diabetes, obesity and dyslipidemia; removing the non-significant values of the model, obtaining the following final equation:

$$\text{Score} = -511 - 156 * \text{gender} + 13.1 * \text{age} + 2.89 * \text{liver UH}$$

Calcium score	Coefficient	SE	t	P>t	[Confidence interval 95%]	
HU	3,105	1,574	1.97	0.040	0.003	6,208
Age	12,158	1,834	6.63	0.000	8,543	15,774
Gender	-139,981	49,162	-2.85	0.005	-236,888	-43,074
Diabetes	-104,119	75,197	-1.38	0.168	-252,346	44,107
Dyslipidemia	42,857	43,425	0.99	0.325	-42,742	128,457
Obesity	4,830	54,622	0.09	0.930	-102,839	112,501
HTN	68,355	44,628	1.53	0.127	-19,614	156,325

Figure 3. *Regression coefficients showing statistically significant association between higher calcium score values and the presence of lower attenuation value of the liver parenchyma, older age and male gender.*

Figura 4.
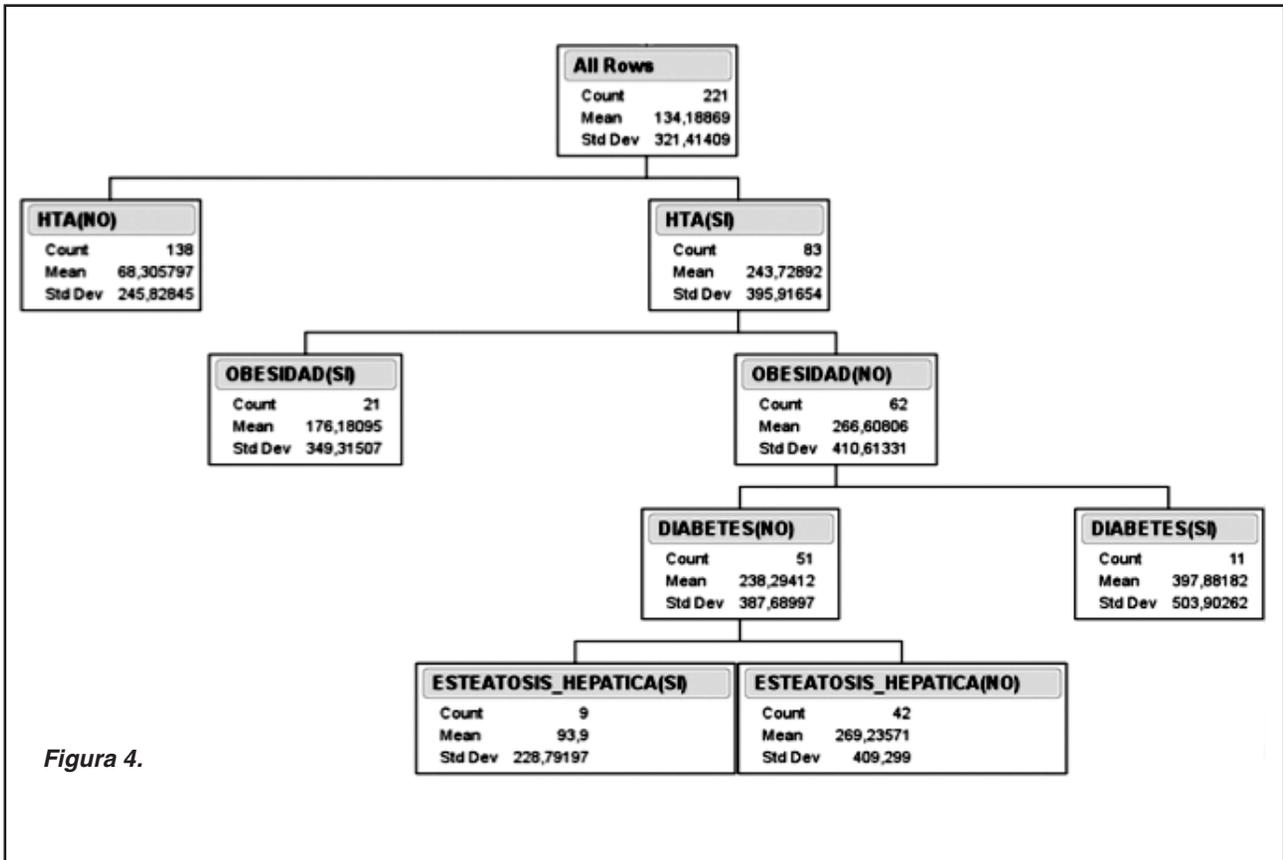
Demonstrating that patients with lower levels of hepatic attenuation and older age, have higher levels of calcium score.

The CART technique relies on the fact that the combination of risk factors for a disease are unique to a particular patient, but have a limited number of combinations in the population. So when you have a large number of patients and variables, you can see which of these combinations bring together the patients with increased risk of disease (Figure 4).

Thus, in this case, 2 groups of patients with the higher levels of calcium score (which have higher coronary risk), were established: One group with arterial hypertension and hepatic steatosis and a second group with arterial hypertension and type 2 DM (Figure 5).

The patients who were only obese did not have higher levels of calcium score.

Discussion

The Agatston Index (score), generally expresses the magnitude of calcium deposited in the coronary tree, establishing a threshold density in HU and its expression in adjacent mass. Calcium, as an alternate expression of the coronary atherosclerotic burden of the subject, is of great epidemiological and prognostic relevance. Thus, Rumberger, *et al*[6] shows that a coronary calcium score (SCC) higher than 371 has a 90% specificity for at least one coronary lesion
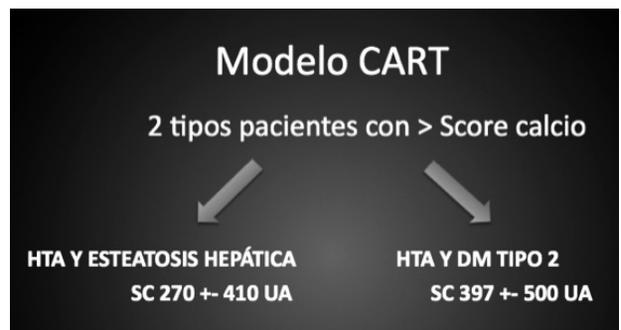

Figura 5.

with stenosis higher than 70%. Coronary calcium scores higher than 1000 are those that have greater probability of acute coronary syndromes. The MESA study (Multi-Ethnic Study of Atherosclerosis) has demonstrated that models which include race, gender and age associated to the absolute calcium score value, are predictors of adverse events[7].

With this study we demonstrated that a statistically significant association exists in the group of patients studied, between the presence of calcified coronary atheromatous and the hepatic steatosis presence, this is probably secondary in that the hepatic steatosis occurs in metabolic syndromes of longer evolution.

Since the patients with hepatic steatosis, as part of a metabolic syndrome, are at increased risk of atherosclerosis, it may be useful to incorporate the

assessment of hepatic steatosis in cardiovascular risk stratification, considering also that this information is available in the standard acquisition of coronary artery computed tomography and calcium score measurements, and does not increase the acquisition time of the examination or exposure to ionizing radiation.

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