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ORIGINAL

Coronary artery calcium quantification with non-ECG-gated low-dose CT of the chest

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KEYWORDS
Computed tomography;
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Abstract
Objective: To evaluate the feasibility of quantifying coronary artery calcification in low-radiation dose chest CT (LDCT) studies performed in an early lung cancer detection program by comparing the results of this technique with those of dedicated retrospectively ECG-gated cardiac CT.
Material and methods: After obtaining informed consent, we evaluated the CT studies of 48 consecutive asymptomatic smokers (44 male, 4 female; mean age 59.7 years) included in an early lung cancer detection trial who underwent multislice LDCT (Volume Zoom, Siemens) of the chest and a retrospectively ECG-gated cardiac CT specifically dedicated to quantifying coronary artery calcification. LDCT examinations were reconstructed to reproduce cardiac CT parameters. Coronary calcium values were compared using the Wilcoxon signed-rank test. The concordance correlation coefficient (CCC) was calculated to determine the agreement between the two methods.
Results: Coronary calcium values ranged from 0 to 1,908.4 (median: 89.6; IQR: 3.2; 227.4) in LDCT exams and from 0 to 1,486.6 (median: 81.3; IQR: 2.5; 316.4) in cardiac CT studies. No statistically significant difference was observed in the estimation of total coronary calcium score ($p = 0.28$). The concordance between the two techniques was excellent (CCC $\geq$ 0.81).
Conclusion: The LDCT study performed in lung cancer early detection trials enables coronary artery calcification to be quantified with the same accuracy as the dedicated retrospectively ECG-gated cardiac CT examination.

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PALABRAS CLAVE
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Radiación

Cuantificación de la calcificación coronaria en tomografía computarizada torácida de baja dosis de radiación sin sincronización cardiaca

Resumen
Objetivo: Evaluar la posibilidad de cuantificar la calcificación coronaria en las tomografías computarizadas (TC) de baja dosis de radiación (TCBD) torácicas realizadas en un programa de detección precoz de cáncer de pulmón con respecto al protocolo cardíaco específico realizado con sincronización electrocardiográfica (ECG) retrospectiva.
Material y métodos: Tras obtener el consentimiento informado se analizaron las exploraciones de 48 fumadores asintomáticos consecutivos (44 varones, 4 mujeres; edad media 59,7 años) incluidos en un programa de detección precoz de cáncer de pulmón a los que se realizó TCBD torácica y un estudio cardíaco específicamente dirigido a cuantificar la calcificación coronaria con sincronización ECG retrospectiva en un equipo TC multicorte (Volume Zoom, Siemens). La exploración TC de baja dosis de radiación se reconstruyó para reproducir los parámetros del estudio cardíaco. Los valores de calcio coronario se compararon con el test de Wilcoxon. Se calculó el coeficiente de correlación de concordancia (CCC) para determinar la concordancia entre ambos métodos.
Resultados: Los valores del calcio coronario oscilaron entre 0 y 1.908,4 (mediana: 89,6; amplitud intercuartil [AIC]: 3,2; 227,4) en TCBD y entre 0 y 1.486,6 (mediana: 81,3; AIC: 2,5; 316,4) en los estudios cardíacos. No se observaron diferencias estadísticamente significativas en la estimación total de calcio coronario ($p = 0,28$). La concordancia entre ambas técnicas fue buena ($CCC \geq 0,81$).
Conclusión: Los estudios de TC de baja dosis de radiación realizados en programas de detección precoz de cáncer de pulmón permiten cuantificar la calcificación coronaria con la misma exactitud que el protocolo cardíaco específico realizado con sincronización ECG retrospectiva.

Introduction

Lung cancer and coronary artery disease are the leading causes of death in developed countries.[1] In 2000, the estimated incidence of lung cancer in Spain was 16,821 cases in men and 1,552 cases in women, with an estimated mortality of 15,974 men and 1,694 women.[2] In 2002, incidence rates of acute myocardial infarctions in people aged between 25 and 74 were 135-210 cases per 100,000 men per year and 29-61 cases per 100,000 women per year,[3-5] with annual ischemic cardiopathy mortality rates adjusted for age and gender of 92.02/100,000 for men and 40.13/100,000 for women.[6] Conventional coronary angiography and echocardiography are the reference standards for studying coronary arteriosclerosis.[7] However, instead of treatment with high-cost invasive procedures, non-invasive techniques are being developed that allow identification of individuals with elevated risk of experiencing a cardiac episode. Among these is Multi-Slice Computed Tomography (MSCT). This technique has proven to be useful for detecting and quantifying coronary calcification,[8] a parameter that stratifies cardiovascular risk and provides prognostic value.[9] Today, evaluation of coronary calcification is performed in an increasing number of hospitals. Moreover, the use of low-dose CT as a screening tool for the early detection of lung cancer has been shown to increase patient survival.[10] Thus, MSCT can be a very useful technique for both diagnosing lung cancer in its early stages and detecting and quantifying the calcification of coronary arteries. However, unlike conventional thoracic studies, quantifying coronary calcification using MSCT requires ECG (electrocardiogram) gating, which implies a greater radiation dose. This study was performed with the hypothesis that using MSCT, a single, low-dose scan can be used to detect lung cancer and quantify coronary calcification. We evaluated the possibility of quantifying coronary calcification using conventional non-ECG-gated low-dose thoracic studies that were performed on asymptomatic consecutive smokers participating in the early detection program for lung cancer being developed at our center. We compared the results with those obtained from ECG-gated studies designed for quantifying coronary calcification.

Material and methods

After obtaining informed consent, 48 asymptomatic consecutive smokers who participate in the early detection program for lung cancer at our center underwent a low-dose CT of the chest and a cardiac CT with retrospective ECG gating.

Protocol of Multi-Slice Computed Tomography

The studies were performed on MSCT equipment with 4-slice detectors (Somatom Volume Zoom, Siemens Medical

Solutions, Erlangen, Germany). The low-dose thoracic studies were performed with the following parameters: 120 kV, 20 mAs, 1 mm slice thickness, 1 mm collimation, 0.7 mm reconstruction increment. For the cardiac studies with retrospective ECG gating, a conventional protocol was used: 120 kV, 133 mAs, 3 mm slice thickness, 2.5 mm collimation, 3.75 mm table movement, 0.5 s gantry rotation time, 1.5 mm reconstruction increment, and B35 reconstruction algorithm. The raw data from the thoracic scan were also reconstructed using parameters equivalent to those of the cardiac study (slice thickness, reconstruction increment, and algorithm) so as to make the two studies comparable. The amount of coronary calcium (Agatston's score) was estimated using commercial software (CaScoring, Siemens Medical Solutions) (fig. 1). Two radiologists independently analyzed the studies, paying special attention to increased image noise and to the pulsatility artifact in the low-dose chest CT scans, to avoid including erroneous pixels in the calculation of coronary calcium. In instances of increased image noise, pixels that followed the vascular route were quantified. In cases of pulsatility artifacts, only the coronary segment that followed the natural route of the coronary vessel was considered, excluding the artifact.

Statistical Analysis

The Shapiro-Wilk test was used as a normality measure. Given that the variables did not follow a normal distribution, the Wilcoxon test was used to compare the amount of coronary calcium in the two scans. The concordance correlation coefficient (CCC)[11] and Bland–Altman plots[12] were used to analyze the agreement between the two CT protocols for estimating the overall score of coronary calcium and the quantity of calcium in each coronary artery. The CCC can present values from 0 to 1; 0 indicates that there is no agreement and 1 indicates perfect agreement. Additional analyses were performed stratifying by age, gender, and heart rate. A value of $p < 0.01$ was considered statistically significant.

Results

Prospective studies of 48 asymptomatic consecutive smokers were analyzed (44 males and 4 females; mean age: 59.7 years; standard deviation [SD]: 8.2; range: 44-83 years). The average heart rate of people in the study at the time of the scan was 69.1 (SD: 12.5) beats per minute. All studies were of diagnostic quality.

Quantification of Coronary Calcium

The values of coronary calcium quantified using low-dose chest CT varied between 0 and 1,908.4 with a median of 0 (interquartile range [IQR]: 0; 0.15) for the left main trunk; 33.2 (IQR: 0; 143.7) for the left anterior descending coronary artery; 4.7 (IQR: 0; 21.8) for the circumflex artery; 0.05 (IQR: 0; 29.2) for the right coronary artery and 89.6 (IQR: 3.2; 227.4) for the total amount of calcium. Coronary calcium values were found between 0 and 1,486.6 in the cardiac studies performed with retrospective ECG gating with a median of 0 (IQR: 0; 0) for the main left trunk; 12.9 (IQR: 0; 102.6) for the left anterior descending coronary artery; 8 (IQR: 0; 53.2) for the circumflex artery; 0.7 (IQR: 0; 32.4) for the right coronary artery and 81.3 (IQR: 2.5; 316.4) for the total amount of calcium. No statistically significant differences were found in the total estimation of coronary calcium ($p = 0.28$) between acquisition techniques (table 1). Coronary calcium was not detected in 8 subjects. Coronary calcium was detected in the low-dose chest CT and not in the ECG-gated cardiac study in only 2 individuals (Agatston values of 0.1 and 4.6).

Concordance between the Scans

The CCC and its 95% confidence interval for the coronary calcium measurements for both acquisition techniques are shown in table. Both scans showed a good agreement in quantifying the coronary calcification, both overall and in each isolated artery, with CCC values ≥ 0.81. There was also good agreement between the techniques in subgroups

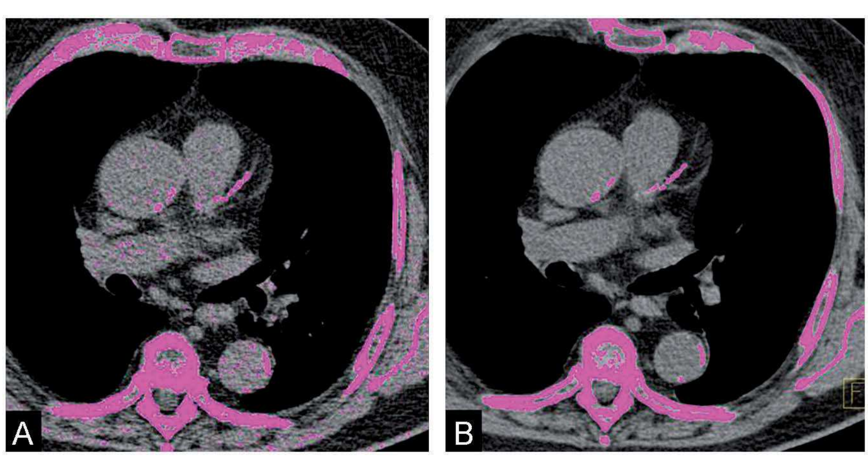

Figure 1 Quantification of coronary calcium A) Axial image obtained with the low-dose protocol B) Axial image obtained with retrospective ECG gating. Calcification is visible in the left anterior descending coronary artery.

Table 1 Analysis of the quantification of coronary calcification for two acquisition techniques

Artery	Low-dose CT Median (IQR)	Cardiac CT Median (IQR)	p*	CCC (CI of 95%)	Bland-Altman Average (CI of 95%)
LMT	0 (0; 0.15)	0 (0; 0)	0.24	0.81 (0.72–0.87)	82.5 (42.1–122.9)
LAD	33.2 (0; 143.7)	12.9 (0; 102.6)	0.09	0.85 (0.75–0.91)	12.6 (—8.3–33.4)
Cx	4.7 (0; 21.8)	8 (0; 53.2)	0.03	0.91 (0.86–0.94)	10.3 (—21.4–41.9)
RCA	0.05 (0; 29.2)	0.7 (0; 32.4)	0.16	0.97 (0.94–0.98)	3.9 (—7.3–15.1)
Total	89.6 (3.2; 227.4)	81.3 (2.5; 316.4)	0.28	0.96 (0.93–0.97)	15.1 (—14.2–44.2)

IQR: Interquartile range; CCC: concordance correlation coefficient; RCA: right coronary artery; Cx: circumflex coronary artery; LAD: left anterior descending coronary artery; CI: confidence interval; LMT: left main trunk.
*Wilcoxon Test.

Table 2 Concordance in estimating total amount of coronary calcium between two computed tomography acquisition techniques according to sex, age and heart rate

Sex		CCC	CI of 95%
	Female (n = 4)	0.95	0.56–0.99
	Male (n = 44)	0.96	0.92–0.98
Age (years)	< 56 (n = 17)	0.88	0.69–0.95
	56–64 (n = 17)	0.96	0.89–0.99
	> 64 (n = 16)	0.96	0.89–0.99
Heart rate (BPM)	< 64 (n = 18)	0.97	0.92–0.99
	64–74 (n = 15)	0.89	0.67–0.96
	> 74 (n = 15)	0.96	0.88–0.99

CCC: concordance correlation coefficient; CI: confidence interval; BPM: beats per minute.

according to age, sex, and heart rate (table 2). Agreement between the measurements of total coronary calcium are shown in a Bland-Altman plot (fig. 2).

Discussion

In past years, screening asymptomatic subjects for detecting latent or early-stage diseases has acquired important socio-epidemiological relevance and has provoked great controversy in the scientific community.[13] Helical CT has been shown to be a potentially useful technique for the early detection of lung cancer;[14] subsequently, the development of multi-slice CT and low-dose protocols (0.65 mSv)[15] have resulted in an increased number of clinical screening studies.[10,16] Moreover, ECG-gated MSCT (radiation dose 1.5-6.2 mSv)[17] has been useful for detecting and quantifying coronary calcification,[8,18,19] a parameter that reflects the total atherosclerotic plaque burden.[20] The coronary calcification holds prognostic value in symptomatic[21] and asymptomatic[22] subjects and, for this reason, its quantification is now recommended for patients with intermediate risk of cardiovascular disease.[23] Given that the same technology (MSCT) is potentially useful for the early detection of lung cancer and estimation of coronary disease risk, performing a single CT scan for both purposes has important clinical relevance. Therefore, the objective of this study was to demonstrate the possibility of quantifying coronary calcification using low-dose CT data collected as part of an early detection program for lung cancer. The results were compared with those calculated from data acquired with a cardiac protocol.

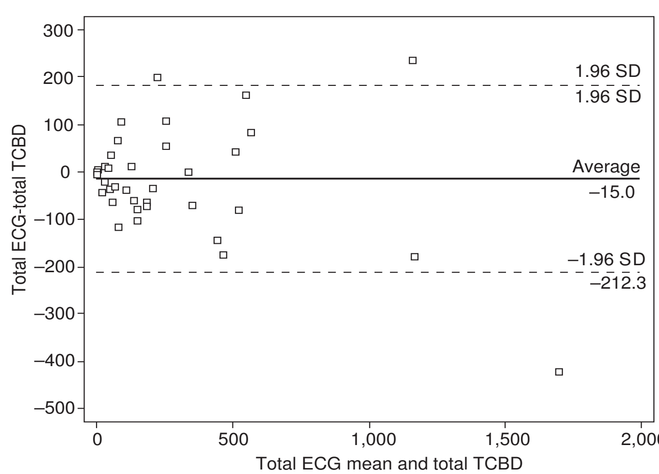

Figure 2 Bland-Altman plot showing the difference in the measurements of total coronary calcium between the retrospective ECG-gated scan and the low-dose CT (LDCT) with respect to the average of the two values. More dispersion is observed as compared with the concordance correlation coefficient (CCC). SD: standard deviation.

In this study, no statistically significant differences were observed in the quantification of coronary calcification between the two acquisition protocols. The median total

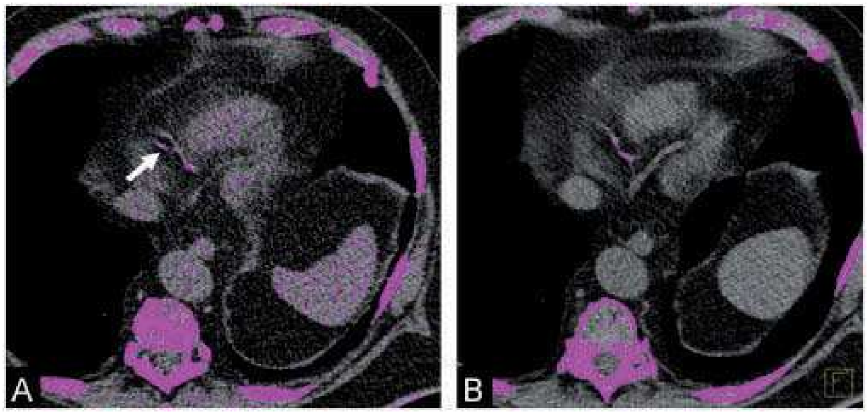

Figure 3 Pulsatility artifact. A) Axial image obtained with the low-dose protocol. B) Axial image obtained with retrospective ECG gating. Note the pulsatility artifact in the right coronary artery (arrow).

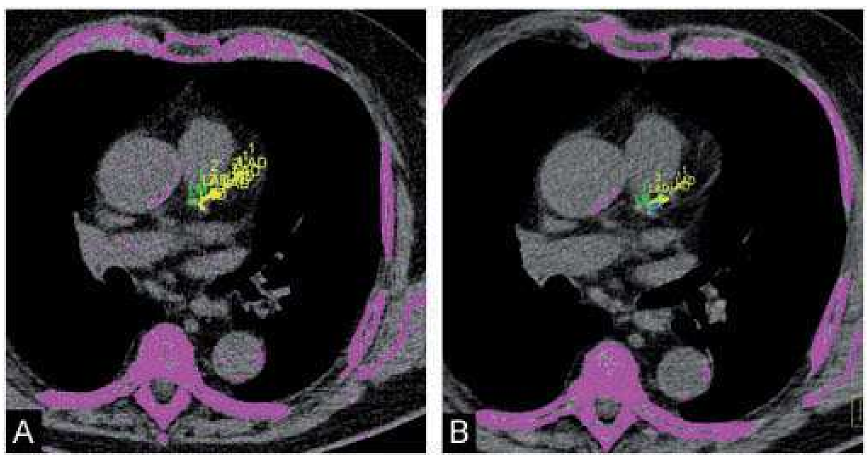

Figure 4 Increased image noise artifact. A) Axial image obtained with the low-dose protocol. B) Axial image obtained with retrospective ECG gating. Note that in the image obtained with the low-dose protocol, because it has more noise, more pixels are detected with density values > 130 HU.

calcium was 89.6 for the low-dose protocol and 81.3 for the ECG-gated acquisition. Both scans showed good agreement for quantifying coronary calcification with CCC values > 0.80, for total calcium and calcium in each artery. Although the confidence intervals were wide due to the small sample size, the CCC showed good agreement. The correlation of the two protocols for quantifying coronary calcification was almost perfect, regardless of the sex, age, or heart rate of the subject. Our study shows that the quantification of the coronary calcification using low-dose thoracic CT and using a cardiac protocol is nearly identical. Therefore, using a low-dose protocol can significantly reduce radiation exposure without deteriorating the estimation of coronary calcification. According to work published by other groups,[24,25] our study also indicates that it is possible to quantify coronary calcification using low-milliamperage CT. The quantity of coronary calcium was estimated using the Agatston scale. Although calculating the volume or mass equivalent to the hydroxyapatite calcium of the atherosclerotic plaque has less variability and correlates more closely with the values obtained from electron beam tomography, a pioneer technique in the quantification of coronary calcification,[26] the Agatston score was used in this study, given that it is traditionally used to stratify cardiovascular risk through CT and is the index upon which clinical recommendations are made.[23,27]

This study has several limitations. A limited number of subjects were included. The two CT protocols acquired data with different slice thicknesses and different radiation doses. To minimize variability when quantifying the coronary calcification, the low-dose studies were reconstructed to approximate the ECG-gated cardiac reconstruction. In this work, it is not possible to determine the effect that changing the reconstruction parameters had on the coronary calcium score. In reconstructing the studies obtained with the low dose protocol, two types of artifacts may have affected the estimation of coronary calcification (cardiac motion artifacts and increased image noise)[28,29] (figs. 3 and 4). The increase in image noise was observed predominately in obese people. The pulsatility artifact appeared in more than half of the subjects, especially near the right coronary artery and in subjects with elevated heart rates. However, none of these artifacts prevented detection and quantification of calcification in any of the coronary segments, allowing estimation of coronary calcification for both protocols. Nonetheless, one of the most important aspects of this work is that there were only two false-positive results (with Agatston values < 5); that is, it detected "calcium" with the low-dose protocol in 2 subjects in whom the standard technique did not demonstrate coronary calcification. This implies that the non-ECG-gated low-dose studies of the chest provide an adequate approximation to the stratification of cardiovascular risk according to the Agatston score. It is possible that the greater temporal resolution possible with the newest generation MSCT equipment can diminish these artifacts. To quantify the coronary calcification, the retrospective ECG gating was used instead of prospective ECG gating because the former is more robust, improves the reproducibility of the quantification, especially in instances of small plaques, and is less variable between scans.[30] It is possible that greater spatial and temporal resolution possible with CT equipment with larger mulit-slice detectors will encourage studies with prospective ECG gating, largely due to the significantly lower radiation dose.[17]

In conclusion, low-dose CT performed with a multi-slice scanner with 4-slice detectors allows the quantification of coronary calcification with nearly the same accuracy as using a dedicated cardiac protocol with retrospective ECG gating. According to these results, it may be feasible to screen for lung cancer and determine the risk of coronary disease using a single low-dose CT scan. However, these results are preliminary and require further study with a larger number of subjects to obtain definite conclusions.

Conflicts of Interest

Dr. Bastarrika declares that he receives support from General Electric, Medrad and Siemens.

Authorship

Study design: Bastarrika, Alonso, Cosín.

Drafting and critical revision of the work: Bastarrika, Saiz-Mendiguren, Arias.

All authors have read the final version of the manuscript and given their approval.

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