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Ordinal Scoring of Coronary Artery Calcifications on Low-Dose CT Scans of the Chest is Predictive of Death from Cardiovascular Disease¹

Purpose:

To assess the usefulness of ordinal scoring of the visual assessment of coronary artery calcification (CAC) on low-dose computed tomographic (CT) scans of the chest in the prediction of cardiovascular death.

Materials and Methods:

All participants consented to low-dose CT screening according to an institutional review board-approved protocol. The amount of CAC was assessed on ungated low-dose CT scans of the chest obtained between June 2000 and December 2005 in a cohort of 8782 smokers aged 40–85 years. The four main coronary arteries were visually scored, and each participant received a CAC score of 0–12. The date and cause of death was obtained by using the National Death Index. Follow-up time (median, 72.3 months; range, 0.3–91.9 months) was calculated as the time between CT and death, loss to follow-up, or December 31, 2007, whichever came first. Logistic regression analysis was used to determine the risk of mortality according to CAC category adjusted for age, pack-years of cigarette smoking, and sex. The same analysis to determine the hazard ratio for survival from cardiac death was performed by using Cox regression analysis.

Results:

The rate of cardiovascular deaths increased with an increasing CAC score and was 1.2% (43 of 3573 subjects) for a score of 0, 1.8% (66 of 3569 subjects) for a score of 1–3, 5.0% (51 of 1015 subjects) for a score of 4–6, and 5.3% (33 of 625 subjects) for a score of 7–12. With use of subjects with a CAC score of 0 as the reference group, a CAC score of at least 4 was a significant predictor of cardiovascular death (odds ratio [OR], 4.7; 95% confidence interval: 3.3, 6.8; $P < .0001$); when adjusted for sex, age, and pack-years of smoking, the CAC score remained significant (OR, 2.1; 95% confidence interval: 1.4, 3.1; $P = .0002$).

Conclusion:

Visual assessment of CAC on low-dose CT scans provides clinically relevant quantitative information as to cardiovascular death.

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Smoking increases the risk for atherosclerotic disease, chronic obstructive pulmonary disease, and lung cancer. Lung cancer screening programs with ungated low-dose multi-detector row computed tomography (CT) are now under way to study the benefit of early diagnosis of lung cancer, and these scans can be used to simultaneously assess coronary artery calcification (CAC) (1–3). We have found that CAC can be quantified from these images by using an ordinal visual scale (4). Even though the low-dose protocol was optimized for lung nodule detection, we found it reliable for CAC categorization of the four major Agatston score categories (5). Furthermore, the clinical value of this visual CAC score was found to be in accord with the results obtained by using the dedicated Agatston CAC score as generated with both electron-beam CT (6,7) and multi-detector row CT (8–11).

CAC is specifically related to atherosclerosis, and its extent is a good marker of the total burden of coronary atherosclerosis (12). The prognostic value of CAC score for cardiovascular events and all-cause mortality was confirmed with large prospective studies of different populations and ethnicities (13–27).

Objectivo

to assess the usefulness of ordinal scoring of the visual assessment of CAC on low-dose CT scans of the chest in the prediction of cardiovascular death.

Amostra

from a prospective cohort of 8782 men and women at high risk for lung cancer who underwent low-dose CT screening for lung cancer in New York State between June 2000 and December 2005. This cohort included subjects who were 40 years of age or older at the time of enrollment. In accordance with the pro-

TC

Imaging and Reading of the Images

Low-dose CT was performed at 140 kVp or less and at 80 mAs or less by using a multi-detector row CT scanner in four institutions and a single-section CT scanner in eight. The CT scan was ob-

ated herein, the section thickness was 1.25 mm or less for 2640, between 2 and 4 mm for 2748, and 5 mm for the remaining 3394. Neither cardiac gating nor intravenous contrast material was used.

The interpretations used herein were all performed at the coordinating center. The scans were initially reviewed by

Interpretação



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Visual Scale for CAC Scoring

Each of the four main coronary arteries was identified (left main, left anterior descending, circumflex, and right). Calcification in each artery was categorized as absent, mild, moderate, or severe and scored by the radiologist as 0, 1, 2, or 3, respectively. Calcification was classified as mild when less than one-third of the length of the entire artery showed calcification, moderate when one-third to two-thirds of the artery showed calcification, and severe when more than two-thirds of the artery showed calcification. With four arteries thus scored, each subject received a CAC score ranging from 0 to 12. For purposes of this analysis, the four categories of CAC were as follows: 0, 1-3, 4-6, and 7-12.

Tronco comum, DA, CX,
CD

0: ausente

1: ligeiro; até 1/3 do vaso

2: moderado; 1/3 a 2/3

3: severo: > 2/3

Total: 0 a 12 pontos

4 categorias

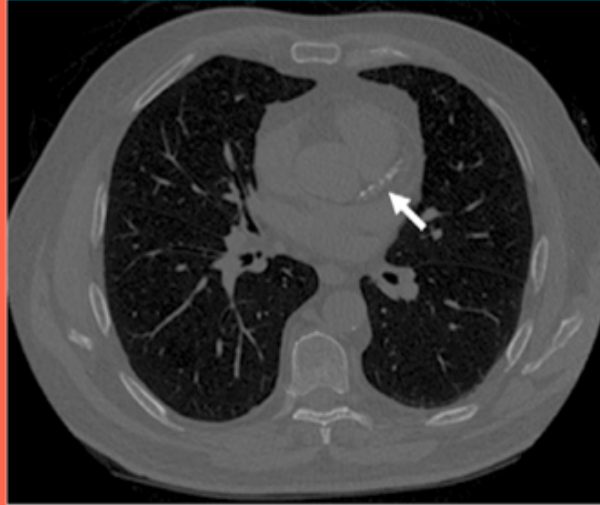


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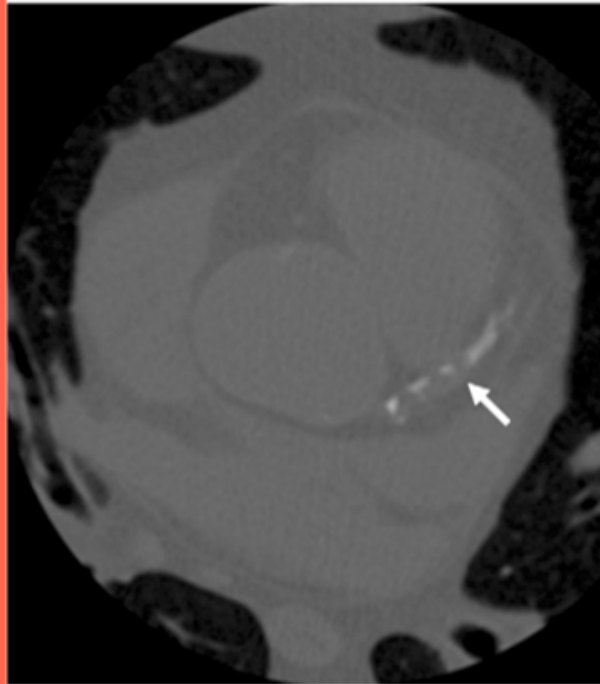
doente 1

doente 2

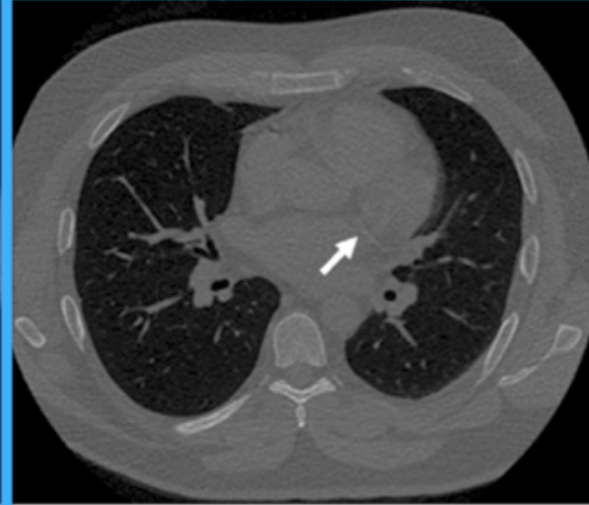
Figure 1



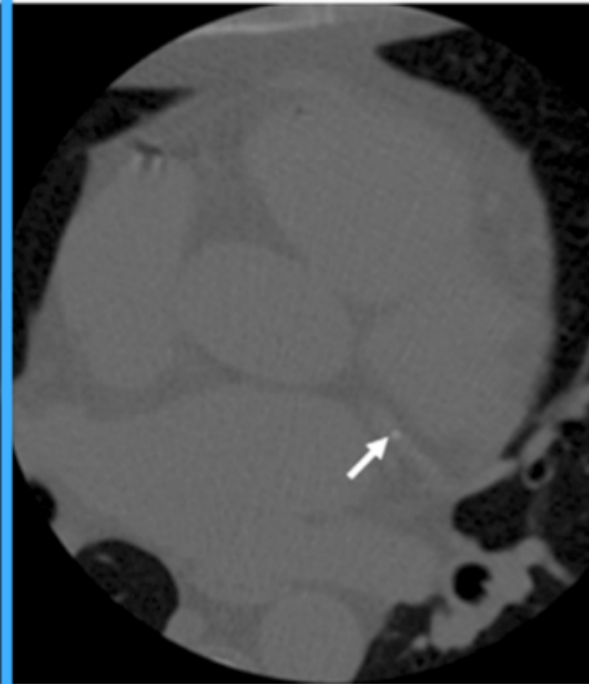
a.



b.



c.



d.

Reprodutibilidade
da escala ordinal

Acuidade

Hábitos tabágicos

Estado vital

Fim do follow-up: 31.12.2007

To determine the interreader consistency for scoring CAC on low-dose CT scans, two radiologists (D.F.Y. and

To understand the accuracy of ungated low-dose CT in depicting coronary calcifications, we reviewed 16 gated regular-dose and ungated low-dose CT scans spanning the entire range of CAC scores. We found excellent correlation ($R = 0.84$, $P < .0001$) between our CAC

Pack-Years of Cigarette Smoking

Detailed information about smoking history was obtained at baseline screening

criteria. The final determination of vital status was obtained by combining information from family members, the participant's physician, and the result from the National Death Index search. For

I-00 to I-78. Follow-up time was calculated from the time of CT to the time of death, loss to follow-up, or December 31, 2007, whichever came first.



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Table 1

Summary of Clinical Characteristics according to Sex

Parameter	Men (<i>n</i> = 4294)*	Women (<i>n</i> = 4488)*	<i>P</i> Value
Age (y) [†]			
Median	64.9 (40–85)	64.8 (40–85)	...
Mean ± SD	65.2 ± 7.1	65.0 ± 7.1	.12
Pack-years [‡]			
Median	45.0 (0.5–315)	42.0 (0.6–282)	...
Mean ± SD	50.7 ± 30.1	45.6 ± 25.7	<.0001
CAC score			<.0001 [‡]
0	1323 (30.8)	2250 (50.1)	
1–3	1909 (44.5)	1660 (37.0)	...
4–7	638 (14.9)	377 (8.4)	...
8–12	424 (9.9)	201 (4.5)	...
Diabetes mellitus	395 (9.2)	227 (5.1)	<.0001

* Except where indicated, data are given as numbers of patients, with percentages given in parentheses.

[†] Numbers in parentheses are ranges. SD = standard deviation.

[‡] Applies to comparison of men and women for all CAC scores.



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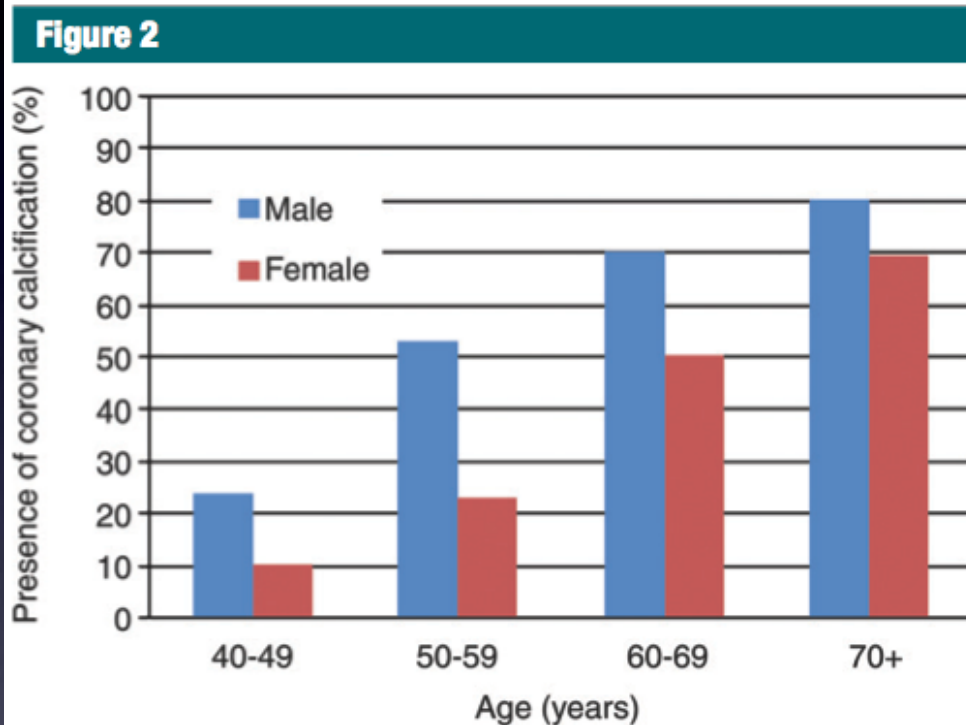


Figure 2: Bar chart shows the frequency of CAC in men and women according to age.

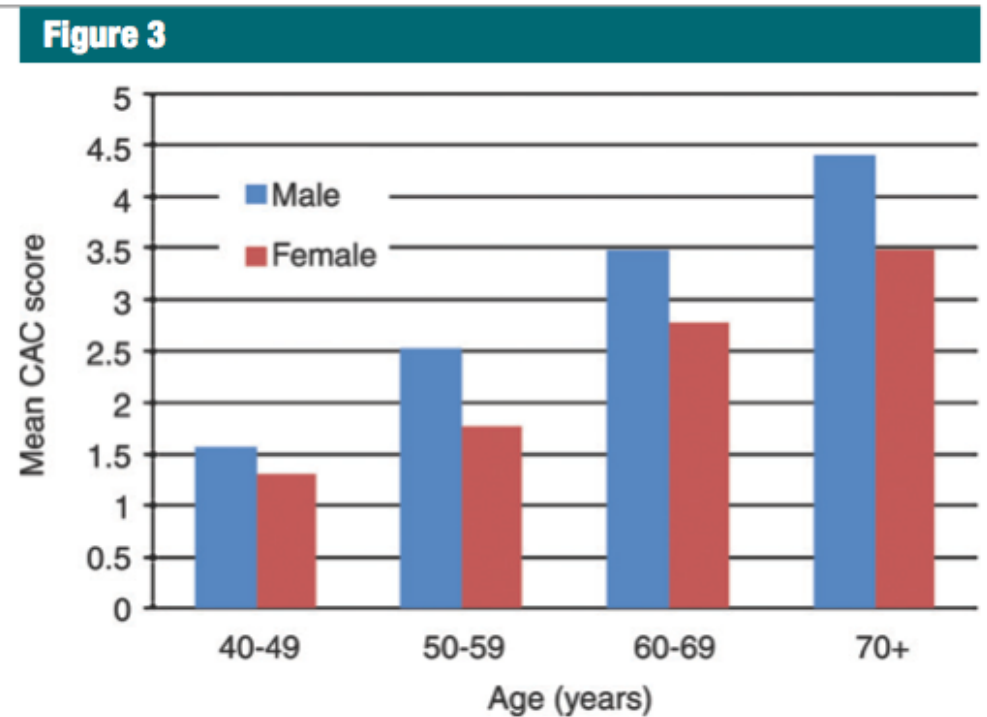


Figure 3: Bar chart shows the mean CAC score (if CAC is present) in men and women according to decade of age.



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Table 2**Characteristics of Those Who Died of a Cardiovascular Event and Those Who Did Not**

Parameter	Died of Cardiovascular Event (<i>n</i> = 193)*	Alive or Died of Noncardiovascular- related Cause (<i>n</i> = 8589)*	<i>P</i> Value
Sex			<.0001†
Men	122 (63.2)	4172 (48.6)	
Women	71 (36.8)	4417 (51.4)	...
Median age (y)‡	72 (49–85)	65 (40–85)	<.0001
Median pack-years‡	50 (10–190)	44 (1–315)	<.0001
Diabetes mellitus	35 (18.1)	587 (6.8)	<.0001

* Except where indicated, data are numbers of subjects, with percentages in parentheses.

† Obtained with the χ^2 test performed to assess whether death from cardiovascular events was different between men and women.

‡ Numbers in parentheses are ranges.



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TM 5%

“ligeira calc em cada uma das art”

Table 3

Mortality Rate and Unadjusted and Adjusted Cox Regression Hazard Ratio according to CAC Category

Parameter	Category 0 (n = 3573)	Category 1–3 (n = 3569)	Category 4–12 (n = 1640)
Mortality rate*	43 (1.2)	66 (1.8)	84 (5.1)
Cox hazard ratio†			
Unadjusted	NA‡	1.6 (1.1, 2.4)§	4.7 (3.3, 6.8)
Adjusted#	NA‡	1.0 (0.7, 1.5)	2.1 (1.4, 3.1)§

* Data are numbers of subjects. Numbers in parentheses are percentages.

† Numbers in parentheses are the 95% confidence interval.

‡ NA = not applicable, this category was used as the reference category to which the other categories were compared.

§ $P < .05$.

|| $P < .0001$.

Adjusted for age, sex, pack-years of smoking, and diabetes.

RR 2X



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Valor prognóstico das calcificações coronárias

Valores mais elevados: homens; aumenta com a idade; aumenta com os hábitos tabágicos

Discussion

The main finding of this study is that CAC score as generated from an ungated low-dose CT scan of the chest provides prognostic information regarding cardiovascular death, even when adjusted for age and smoking history; moderate

It has been previously shown that the visual ordinal scale scoring of CAC on ungated low-dose CT scans provides clinically relevant information (4). With use of this scale, higher CAC scores were identified in men than in women, along with increased scores with increasing age and pack-years of smoking for both men and women. Wu et al (5) compared the concordance of CAC scores on low-dose ungated and regular-dose electrocardiographically gated multi-detector row CT scans and found that low-dose ungated multi-detector row CT when compared with an optimized protocol is reliable for predicting the presence of CAC and the categorization of the four major Agatston score categories. It was also demonstrated



Avaliação incompleta factores de risco cardiovascular

População de elevado risco
(tabagismo)

The main limitation of the present study is the inability to assess the Framingham cardiovascular risk. Because our cohort consisted of participants in a lung cancer screening program, cardiovascular risk factors were not fully registered at baseline. We also did not evaluate the effect of CAC on acute myocardial infarction. However, recently reported prospective studies, all with measured risk factors, consistently demonstrated the independent and incremental prognostic value of CAC measurement over the Framingham risk stratification for cardiac events and all-cause mortality. Our results are not representative of the entire population at risk for cardiovascular death; however, given the high prevalence of smoking worldwide it does represent a large subgroup at high risk of mortality from the current leading causes of death. Because we used ungated CT scans, there may be blurring of the CAC and thus small subtle calcifications may be missed (4,5,32). Although



Advance in Knowledge

- Ordinal scoring of the extent of coronary artery calcification (CAC) on ungated low-dose CT scans is useful because a high score is a significant predictor of cardiovascular death.

Implication for Patient Care

- Ordinal scaling of CAC provides useful prognostic information and should be provided in the interpretation of chest CT scans.

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CD

0: ausente

1: ligeiro; até 1/3 do vaso

2: moderado; 1/3 a 2/3

3: severo: > 2/3