Distribution of Coronary Artery Calcium Scores Determined by Ultrafast Computed Tomography in 2.253 Asymptomatic White Men

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Objective - *To describe the distribution of coronary artery calcium scores in a population of asymptomatic white Brazilian men undergoing assessment with ultrafast computed tomography.*

Methods - *The study assessed 2.253 men aged 22 to 88 years undergoing computed tomography in an Imatron[R] C150 device for detecting coronary calcium. Data were divided based on the patient's age into 7 groups: < 40 years, 40-44 years, 45-49 years, 50-54 years, 55-59 years, 60-64 years, and >65 years.*

Results - *The mean and standard deviation of age were 50.0 ± 9.7 years. In 48.8% of the cases, the coronary artery calcium score was > zero, with a non-Gaussian distribution and a large variation for the same age group. A direct correlation between age and the coronary artery calcium score was observed (r=0.4, P<0.01). Except for the comparison of individuals in the age groups 60-64 years, below 55-60 years, and above 65 years, the older the age group, the greater the medians of the coronary artery calcium scores (P<0.0001). Coronary artery calcium scores were reported according to the 25th, 50th, 75th, and 90th percentiles for the age groups.*

Conclusion - *This study, the first to report the distribution of the coronary artery calcium scores in a sample of white Brazilian men, may be useful for stratifying the risk of coronary events.*

Keywords: electron beam computed tomography, coronary artery disease, diagnosis

Coronary atherosclerosis is one of the major causes of death among us [1]. Atherosclerosis is a multifactorial disease, and the identification of individuals at high risk for coronary events is extremely important, because preventive therapies, such as change in lifestyle and use of drugs, such as statins and acetylsalicylic acid, significantly reduce clinical events and mortality [2]. Classically, the risk stratification of coronary events has been performed through the analysis of a set of risk factors. However, epidemiological data have shown that approximately 25% of the individuals who died suddenly due to cardiac causes had no previous symptoms, and even the classical tools for assessing the risk of coronary events, such as the Framingham scores, have limitations in identifying high-risk individuals [3,4]. Approximately 50% of the coronary deaths and most myocardial infarctions occur in individuals considered at low to intermediate risk, according to clinical and laboratory parameters [3]. Therefore, assessment of subclinical atherosclerosis through imaging techniques may be useful for risk stratification, because evidence exists that the load of the atherosclerotic plaque correlates with the risk of coronary events [5,6].

Coronary artery calcification (fig. 1), detected on ultrafast computed tomography or electron beam computed tomography, correlates with the load of the atherosclerotic plaque in histological, angiographic, and intravascular ultrasound studies [7-10]. Ultrafast computed tomography is a noninvasive and very sensitive method to detect calcification in coronary arteries [7]. Evidence exists that the presence of coronary artery calcification on ultrafast computed tomography may be a risk marker of clinical events in coronary artery disease, independent of the risk factors for atherosclerosis [11-14]. Up to now, coronary artery calcium scores in the Brazilian population have not been reported.

This study aimed at describing the distribution of coronary artery calcium scores in a population sample of asymptomatic white Brazilian men undergoing assessment on ultrafast computed tomography.

Arq Bras Cardiol, volume 81 (supl. VII), 32-6, 2003

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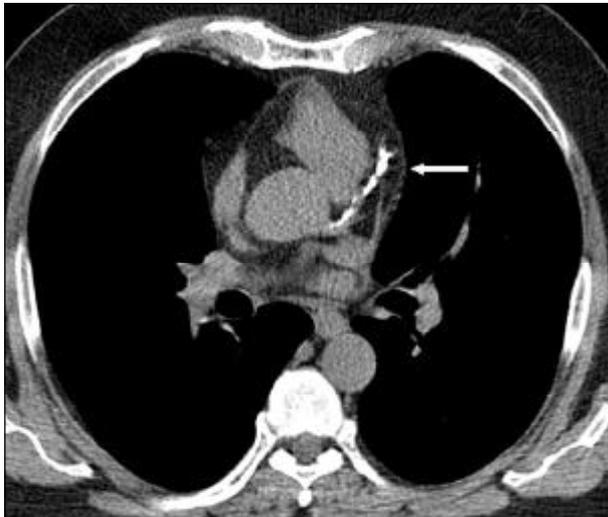Ultrafast computer tomography in assymptomatic white men

Fig. 1 - Calcification of the anterior descending artery detected on ultrafast tomography in an asymptomatic man (arrow).

Methods

This study assessed 2.253 asymptomatic, from the cardiovascular point of view, men undergoing ultrafast computed tomography in the Jardins Diagnostic Unit of the Hospital Israelita Albert Einstein, in São Paulo, from November 1999 to April 2002. The examination was indicated by the physicians on routine assessment. Individuals with a clinical diagnosis of coronary artery disease or undergoing angiography, revascularization with a catheter, or myocardial revascularization were excluded from the study.

The tomographies were performed with an Imatron[R] C-150 tomograph (Imatron Corporation, San Francisco, California, USA), and the images were obtained with 3-mm axial sections of the heart at the end of diastole triggered by the electrocardiography at 100-ms intervals during the inspiratory pause. Coronary artery calcification was considered an image of 2 contiguous pixels with an attenuation coefficient > 130 Hounsfield units. The coronary artery calcium score was calculated according to the Agatston method [15], multiplying the calcification area in square millimeters by a factor 1, 2, 3, or 4, depending on the attenuation coefficients determined by calcium. Factor 1 was used for coefficients between 130 and 199 Hounsfield units; factor 2 for coefficients between 200 and 299 Hounsfield units; factor 3 for coefficients between 300 and 399; and factor 4 for coefficients greater than 400 Hounsfield units. The coronary artery calcium score was the sum of all the scores obtained in all coronary arteries and in all tomographic sections, calculated with Accuscore[R] software (AccuImage Diagnostics Corporation, San Francisco, CA, USA). However, the calculations were only performed after the presence of calcium was confirmed by the operator.

Data were divided based on the patient's age into 7 groups: < 40 years; 40-44 years; 45-49 years; 50-54 years; 55-59 years; 60-64 years; and > 65 years. Descriptive statistics was performed and the means, medians, and standard deviations were calculated in each age group with Microsoft Excel[R] (Microsoft, Brazil) and Sigmastat for Windows[R] (Jandel Scientific, San Rafael, CA, USA) software. The Gaussian or non-Gaussian distributions of data were assessed with the Kolmogorov-Smirnov test. Age was correlated with the values of the coronary artery calcium scores through the Spearman test, and the values of the coronary artery calcium scores were also compared between each other in the different age groups using the analysis of variance for the nonparametric repeated measures (RM-ANOVA) and the Dunn test. The value of 2-tailed $P < 0.05$ was considered significant.

Results

The mean, standard deviation, and age interval were 50 ± 9.7 years (22-88 years). The coronary artery calcium score was > zero in 48.8% of the cases. Table I shows the means, medians, and standard deviations of the coronary artery calcium scores that had a non-Gaussian distribution and showed a great variation for the same age group. A direct correlation between age and the coronary artery calcium score was observed (r=0.4, P<0.01). Except for the comparison between the individuals in the age groups 60-64 years, below 55-60 years, and above 65 years, the older the age group, the greater the medians of the coronary artery calcium scores (P<0.0001). Table II shows the coronary artery calcium scores divided according to the distribution of the 25th, 50th, 75th, and 90th percentiles.

Discussion

The determination of coronary artery calcification with ultrafast tomography has been used in preventive cardiology to assess the risk of coronary events in asymptomatic individuals [7]. The coronary artery calcium scores are a means of systematizing these values with diagnostic and

Table I - Mean, standard deviation, and median of coronary artery calcification according to age in 2.253 asymptomatic white individuals

Age	<40	40-44	45-49	50-54	55-59	60-64	> 65
N	313	392	469	433	305	173	168
Mean	21	51	75	116	159	222	419
SD	110	346	296	299	347	401	829
Median	0	0	0	3	22	68	111

Table II - Distribution of the percentiles of calcification in coronary arteries according to age in 2.253 asymptomatic white individuals

Age	<40	40-44	45-49	50-54	55-59	60-64	>65
N	313	392	469	433	305	173	168
25%	0	0	0	0	0	1	12
50%	0	0	0	4	22	68	112
75%	0	6	25	84	134	276	440
90%	17	58	134	340	462	641	1107

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prognostic intention. This study was the first to describe the coronary artery calcium scores assessed on ultrafast tomography in a Brazilian population sample. Prior to it, descriptions of the coronary artery calcium scores existed only for populations in the USA [3,16,17]. The description of coronary artery calcium scores is necessary in our population, because it is not only the prevalence of coronary artery disease that differs in our country, but also its ethnic composition as cited previously.

The distribution of coronary artery calcium scores greatly varies, and this distribution does not follow the Gaussian curve. The standard deviations are greater than the mean, which makes the classical presentation in the form of mean and standard deviation inappropriate. However, for descriptive purposes, they were listed in table I. Thus, the median would be the better way to depict the data. In all age groups assessed, 50% of the individuals had a score equal to zero, which justifies the values of the medians in table I.

As in other populations, coronary artery calcium scores increased with age [13,16,17]; however, the non-Gaussian distribution and the small number of individuals in the age groups > 60 years in our sample jeopardized the better comparison of coronary artery calcification between that age group and those immediately below and above it. Although the medians are greater, no statistical difference was observed in these values. It is worth stressing that despite this apparent limitation, evidence exists that the greater specificity for detecting the risk for coronary events lies in the assessment of coronary artery calcification between the age groups from 35 to 55 years or to 60 years [7]. In our study, 75% of the individuals were younger than 60 years of age. Although age is an important determinant of the coronary artery calcium score, other risk factors for atherosclerosis, such as smoking, cholesterol, and arterial hypertension, were not assessed in this study and in other studies describing coronary artery calcium scores in populations of the USA with multivariate analysis.

In the images obtained on ultrafast tomography, coronary artery calcification may be easily identified by the density 8-times greater than that of the surrounding tissues [18]. The Imatron[R] ultrafast tomograph differs from the conventional and modern helical ones, because its velocity of image acquisition is 50-100 ms, ie, 3 to 6 times faster, which reduces the risk of artifacts, and makes this device the gold standard for assessing coronary artery calcification [7].

A strong correlation between coronary artery calcification identified on fluoroscopy or on anatomicopathological examination and coronary artery disease has been known since 1961 [19,20]. More recent research has suggested that calcium is already present in the atherosclerotic plaque in its first stages, when the lesion is constituted only by fatty streaks [21]. However, in this stage, calcium cannot be identified by means of the current noninvasive methods. As the lesion progresses with the addition of cholesterol, inflammatory cells, and fibrous tissue, calcium builds up in the form of plaque, in the base of the intima, and becomes iden-

tifiable on ultrafast tomography. Simons et al [22] analyzed sequential histological sections from the initial to the caudal portions of 525 coronary arteries. Although calcium was not present in all lesions, an important correlation was found between the amount of calcium and the degree of atherosclerosis in each coronary artery. Almost all lesions without calcification had no significant obstruction of the coronary lumen, showing that identification of calcium and its quantification allow the evaluation of the degree of existing coronary artery disease. A similar study by Rumberger et al [23], correlating coronary artery calcium quantification on ultrafast tomography in hearts at autopsy and its histopathologic quantification, confirmed these data. Angiographic and coronary artery ultrasound studies have also shown that coronary artery calcification correlates with the load of the atherosclerotic plaque [8-10], and the latter, in turn, correlates with the risk for coronary events [5-6]. Several studies in asymptomatic or symptomatic individuals on coronary artery disease have shown a correlation between coronary artery calcification and obstruction of the lumen of the vessel [9,18,24]. Although the sensitivity of ultrafast tomography for the diagnosis of coronary artery obstruction reaches 95%, its specificity is around 66% [24], a fact that jeopardizes the role of ultrafast tomography in the triage of coronary artery obstructions.

The major usefulness of ultrafast tomography lies in its capacity to identify the risk for coronary events independently of the classical risk factors [3]. North American data have shown that approximately 50% of the coronary events originate in the so-called intermediate risk range, according to the use of clinical data for stratification, such as those of the Framingham table. Therefore, it is necessary that other tests be used for a better stratification of the risks for coronary events. Data from the literature have shown that the presence of coronary artery calcification is associated with a greater risk for coronary events [11-14], and its absence is associated with an almost-zero risk for coronary events in studies of 3-to-5 year follow-up [25]. Coronary artery calcium scores have their major usefulness in stratifying the risk for clinical events. A recent meta-analysis showed that individuals with coronary artery calcium scores above the median had a 4.2-times greater relative risk of death due to coronary artery disease or myocardial infarction (95% CI 1.6-11.13) compared with individuals with coronary artery calcium scores below the median [26]. Evidence indicates that individuals with coronary artery calcium scores above the 67th, 75th, and 80th percentiles for sex and age, which are superior percentiles depending on the case series assessed, had an annual absolute risk for myocardial infarction or death due to coronary artery disease, or both, of 1.8%, 2.3%, and 4.5%, respectively, placing these patients in the high-risk range. Another option proposed in a prospective study for assessing the risk of coronary events was the use of absolute scores and not their distribution according to age and sex [11]. Classically, coronary artery calcium scores above 400 are associated with a greater risk for coronary obstructions and clinical events [27]. Arad et al [11], studying 1,172 indivi-

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duals over 3 years, showed that a coronary artery calcium score > 160 was associated with a 20.2-greater odds ratio of having myocardial infarction or death due to coronary artery disease. These findings did not depend on classical risk factors. However, in a population at high risk for coronary events according to clinical data, the coronary artery calcium scores were not more efficient than the Framingham scores in identifying individuals with clinical events [28]. These data were refuted due to the inappropriate methodology of the examinations performed by Detrano et al [28].

Recently, Grundy [29] has proposed the association of coronary artery calcium scores with the Framingham scores for the risk stratification of coronary events. Age has been known to be one of the major risk markers for coronary events in association with the increase in the load of atherosclerotic plaque. Determination of a higher or lower degree of coronary artery calcification, as an indicator of the amount of atherosclerotic plaque, reduces or increases the points attributed to age in the Framingham tables.

The major criticism of prospective studies with ultrafast tomography is the small number of clinical events occurring during the follow-up, which limits the discriminating power of these studies [25]. Likewise, the indiscriminate use of examinations without a medical indication, based on Bayes' theorem, is criticized because the use of ultrafast tomography in individuals at low clinical risk only exceptionally will identify individuals at high risk for coronary events [30]. Consequently, the costs of an indiscriminate assessment become prohibitive from the public health point of view. The MESA study with more than 6.500 individuals of diverse ethnicities carried out in the USA compared ultrafast tomography, the assessment of the carotid intima/media ratio on ultrasound, and clinical scores of risk to determine whether the noninvasive techniques are superior, complementary, or inferior to the clinical assessment of the risk for coronary event [25].

In conclusion, based on the current literature, when well-indicated, the assessment of coronary artery calcium scores is useful for stratifying coronary risk. Once the individuals at high risk for events are identified, we propose that they be treated according to the current prevention guidelines, mainly in regard to the use of statins and acetylsalicylic acid [2]. We suggest that further studies approach the determination of coronary artery calcium scores in women, assess a greater number of males at more advanced ages and of different social classes than that of the population studied (middle-class individuals). We also suggest that the coronary calcium scores reported for Brazilian populations should be compared with those of populations in the USA, because these are the patterns available in the literature. If differences are found, a prospective study about the value of coronary artery calcification in our population should be carried out. Our study is a starting point. We emphasize, as limitations of our study, the predominance of Caucasians and of middle-class individuals in our population sample. Studies with a greater number of individuals of both sexes, and different ethnicities and social classes are being carried out.

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