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Sfeir M, Matta A, Moussalem N, Kharma A. Valeur du score calcique dans le diagnostic de la maladie coronarienne chez les patients à haut risque et épreuve d'effort négative. *J Med Liban* 2018 ; 66 (3) :150-153.

ABSTRACT • Aim : The significance of the coronary calcium score (CS) as to its correlation to coronary artery disease (CAD) has been well studied, however, its significance in adding information to asymptomatic high risk patients with negative stress test has not been investigated. The aim of our study was to look at this specific population and find out what was the significance of adding CS to a negative stress test. **Materials and methods :** A retrospective study was conducted on 134 consecutive asymptomatic patients who had a stress test, coronary scan and CS in the Cardiovascular Department of Notre-Dame de Secours University Hospital (NDSUH). These patients had to have in addition to a negative stress test at least two risk factors for CAD. Patients with known CAD and those with bad quality coronary scans, or any kind of invasive cardiac procedures, were excluded. Stress test results, coronary scans results and CS were reviewed. For the 2x2 tables analysis, a χ^2 test was used. **Results :** Of the 134 patients, 96 had no significant CAD defined as $\leq 50\%$ luminal stenosis, and 96 had a CS < 40. Of the 96 patients with no significant CAD, 41 (43%) had a CS = 0. Of the 41 without a CS, 39 (95%) had normal coronary arteries. Statistical analysis showed that CS < 40 excludes significant CAD, with a sensitivity of 100% and a specificity of 95.05%, and that normal coronaries could be predicted by a CS = 0 with a sensitivity of 97.5% and a specificity of 96.72%. Note that the mean of CS ≥ 40 for patients with significant CAD on coronary scan is 125.9 ± 99.4 . **Conclusion :** A CS < 40 excludes the presence of significant CAD and a CS = 0 is a highly predictive value of normal coronary arteries ($p < 0.0001$).

Keywords : calcium score; high risk asymptomatic patients; significant coronary artery disease

RÉSUMÉ • Objectif : La relation entre le score calcique (SC) et la maladie coronarienne (MC) a été étudiée, mais sa valeur chez les patients asymptomatiques à haut risque cardiovasculaire ayant une épreuve d'effort normale n'a pas été investiguée. Le but de cette étude rétrospective vise à évaluer cette population spécifique, et à démontrer l'importance d'ajouter le SC à une épreuve d'effort négative. **Méthodes :** Étude rétrospective faite sur une population de 134 patients asymptomatiques référés pour une épreuve d'effort, un scan coronarien et un SC, et choisis consécutivement. En sus de l'épreuve d'effort négative ces patients devaient avoir au moins deux facteurs de risque cardiovasculaire, en excluant ceux connus pour avoir une MC, des scans coronariens de mauvaise qualité, ou tout type de procédures cardiaques invasives. Les résultats des épreuves d'effort et les scores calciques ont été révisés. Pour l'analyse des tables 2x2, le test chi-square a été utilisé. **Résultats :** Parmi les 134 patients, 96 n'avaient pas de maladie coronarienne significative définie par une sténose luminale $\leq 50\%$ et 96 avaient un SC < 40. Parmi les 96 patients n'ayant pas de maladie coronarienne significative, 41 (43%) avaient un SC = 0 dont 39 (95%) avaient des artères coronaires normales. Les analyses statistiques montrent qu'un SC < 40 exclut une maladie coronaire significative avec une sensibilité de 100% et une spécificité de 95,05%, et que les coronaires normales peuvent être prédites par un SC = 0, avec une sensibilité de 97,5% et une spécificité de 96,72%. On note que la valeur moyenne du SC chez les patients avec maladie coronarienne significative sur le coroscan est de $125,9 \pm 99,4$. **Conclusion :** Un SC < 40 exclut la présence d'une maladie coronarienne significative, et un SC = 0 a une valeur prédictive élevée de présence d'artères coronaires normales ($p < 0,0001$).

Mots-clés : score calcique; patients asymptomatiques à haut risque; maladie coronarienne significative

INTRODUCTION

Cardiovascular disease is the leading cause of death worldwide [1]. The calcium score reflects the presence of calcifications on the vessels' wall, and indicates the presence of a higher risk of coronary artery disease (CAD). The most used method for detection and quantification of the calcium plaques is the coronary scan [2-5]. Data concerning the correlation between coronary

calcium score (CS) and CAD in high risk asymptomatic patients with a negative stress test have not been studied. Studies have included symptomatic patients without known CAD [6], or both symptomatic and asymptomatic patients with low cardiovascular risk, and without performing a stress test [7], or included diabetic patients having negative and positive ECG stress tests or positive thallium myocardial scintigraphy [8]. The purpose of our

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study is to discover whether adding a calcium score to a negative stress test in high risk asymptomatic patients will add information as to the presence or absence of coronary disease.

METHODS

A retrospective study of 134 consecutive patients referred to stress test, coronary scan and calcium score in the Cardiovascular Department of Notre-Dame de Secours University Hospital (NDSUH) was conducted.

We reviewed thoroughly the stress tests results for detection of normal ones, the coronary scans for detection of presence or absence of significant CAD or normal coronaries, and the calcium score evaluation.

Stress tests were done and interpreted according to Bruce protocol by the same reference cardiologist in the Cardiovascular Department.

Coronary scans were performed with VCT 64 according to a standardized protocol with a heart rate controlled by β -blockers and were reviewed by the same cardiologist. Patients with acute coronary syndromes, or those having less than two risk factors of CAD and those with positive stress test were excluded. Bad quality coronary scans were excluded. Patients who had already undergone angiography or cardiac surgeries were excluded.

CAD risk factors were defined by the presence of one of the following: diabetes mellitus, dyslipidemia, arterial hypertension, obesity defined by BMI > 30.

The study was approved by the ethics committees of NDSUH and written consent was obtained from the hospital to allow data collection.

The CS is used to relate the coronary plaque burden and a cut-off point at 40 was chosen according to statistical analysis that shows the highest level of

specificity and sensitivity. Significant CAD was defined by the presence of a lesion $\geq 50\%$ in any coronary arteries.

A p value < 0.05 was considered to be significant. For the 2 x 2 table analysis, a chi-square test was used.

RESULTS

One hundred and thirty-four patients with a mean age of 42 years were studied. Table I shows the summary of some demographic data. According to coronary scans results, 101 (75.4%) patients had non significant CAD and 33 (24.6%) had significant CAD (lesion $\geq 50\%$). According to calcium scores, 96 (71.6%) had a CS < 40, and 38 (28.4%) had a CS ≥ 40 . Considering the relationship between a CS < 40 and the absence of significant CAD, among the 96 patients who had CS < 40, 96 patients (100%) had no significant CAD. Five (13.1%) out of the 38 patients with CS ≥ 40 had no significant CAD and 33 (86.8%) did not (Chart 1 & Table II). Considering the presence of normal

TABLE I
PATIENTS DEMOGRAPHIC DATA

Variable	N (%)
Mean age	42 \pm 9 years
Gender	
Male	83 (61.9%)
Female	5 (38.1%)
Smokers	84 (62.7%)
Diabetic patients	35 (26.1%)
Hypertensive patients	89 (66.4%)
Dyslipidemic patients	60 (44.8%)
Familial history of CAD	61 (45.5%)

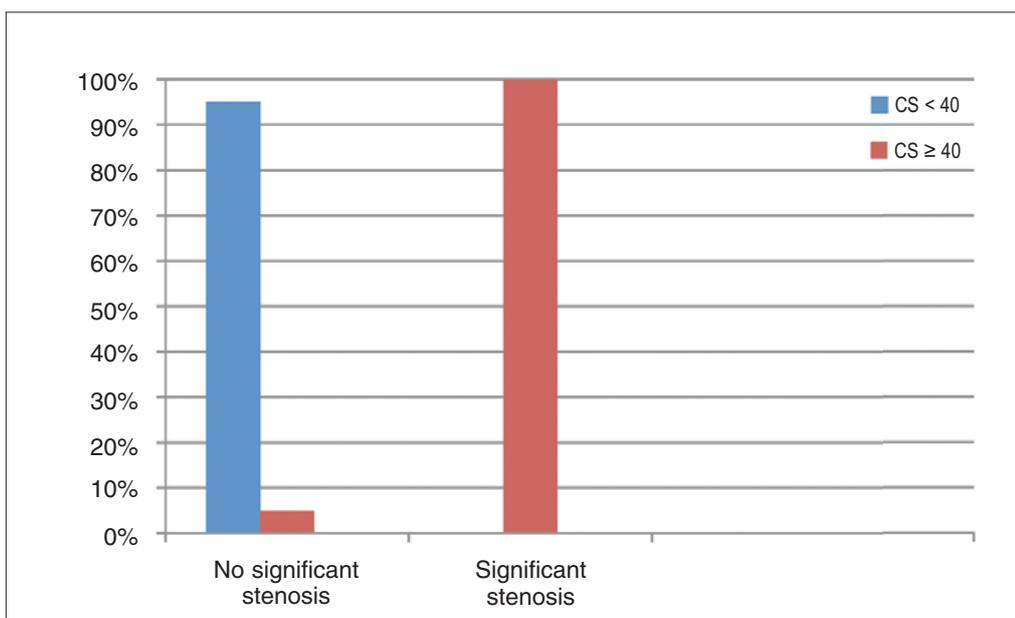


Chart 1

Prevalence of calcium score (CS) < 40 in patients with no significant coronary artery disease (CAD)

TABLE II

CORRELATION BETWEEN CS < 40 & ABSENCE OF SIGNIFICANT CAD

CS < 40	CAD		Patients Total number
	Nonsignificant	Significant	
+	96	0	96
-	5	33	38
Total	101	33	134

CS: calcium score CAD: coronary artery disease OR: infinity
Se: 100% Sp: 95.05% VPP: 86.84% NPV: 100% p < 0.0001

coronaries among the 101 patients with absent significant CAD on the coronary scan, 40 patients (39.6%) had normal coronaries and 61 (60.4%) did not. Thirty-nine (97.5%) out of the 40 patients with normal coronaries on the coronary scan had CS = 0 and 1 (2.5%) did not (CS = 2) (Chart 2 & Table III).

Statistical analysis showed that CS < 40 excludes significant coronary disease with a sensitivity of 100%, a specificity of 95.05%, a positive predictive value of 86.84% and a negative predictive value of 100%, and that normal coronaries can be predicted by CS = 0 with a sensitivity of 97.5%, a specificity of 96.72%, a positive predictive value of 95.12% and a negative predictive value of 98.33%. Statistical results show significant relationship between CS < 40 and absence of significant CAD (OR = infinity), and between CS = 0 and normal coronaries (OR = 1150.5; 95 CI = [100.85; 13125.24]) with p value < 0.0001.

DISCUSSION

Our study is unique in that it's the first one that has been conducted to find a cutoff point below which there is no

TABLE III

CORRELATION BETWEEN CS = 0 & NORMAL CORONARIES

CS = 0	Normal coronaries	Nonsignificant stenosis (< 50%)	Patients Total number
+	39	2	41
-	1	59	60
Total	40	61	101

CS: calcium score OR: 1150.5 CI: [100.85; 13125.24] Se: 97.5%
Sp: 96.72% VPP: 95.12% NPV: 98.33% p < 0.0001

significant CAD in the population we studied. CS < 40 excludes significant CAD in asymptomatic high cardiovascular risk patients, that have otherwise a normal stress test and no known structural heart disease as in the population we studied above; so these patients don't need further investigations unless they become symptomatic. A simple follow-up is sufficient in that category of patients. Moreover, CS = 0 can be a sign of normal coronaries. Concerning patients with CS ≥ 40, they necessitate further investigations to confirm the presence or absence of CAD. Studies done before have controversial results.

Laurence *et al.* have studied asymptomatic patients using electron beam computed tomography (EBCT), but without performing a stress test, and found that patients ≥ 50 years having a CS ≥ 200 and those < 50 years with a CS ≥ 100 have significant CAD [8]. Villines *et al.* looked for a CS = 0 in 10037 symptomatic patients without known CAD that had undergone coronarography and CS, and found a prevalence of 3.5% of significant CAD, a lower negative predictive value than our study for a CS = 0 and 50% coronary stenosis [6]; this is probably because of the different population that we have studied,

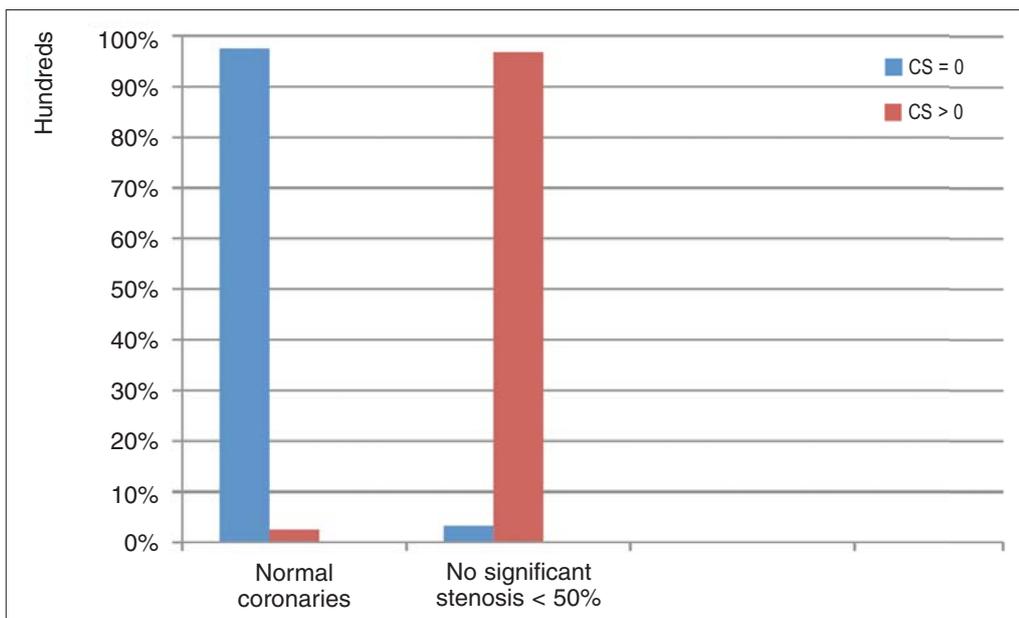


Chart 2

Prevalence of calcium score (CS) = 0 in patients with normal coronaries

and the less strict exclusion criteria in Villines *et al.* study dealing with symptomatic patients. We excluded symptomatic patients and those with positive stress test. Sarwar *et al.* included in their systematic review both symptomatic and asymptomatic patients with low cardiovascular risk; they found a significant relation between a CS = 0 and absence of occurrence of cardiovascular event during 51 months of follow-up: only 0.56% of asymptomatic patients with CS = 0 had a cardiovascular event [7]; this value is higher than that in our study which shows that 0% of patients with CS = 0 had significant CAD. This is probably related to the strict exclusion criteria in our study which only kept the asymptomatic patients at high cardiovascular risk with negative stress test. Dupuy *et al.* conducted a study including diabetic patients: 34 patients had a negative stress test, 14 had a positive stress test or positive thallium myocardial scintigraphy. Of the 11 diabetic patients having a CS between 10 and 100, three coronarographies were done: two were normal, and one had shown a tritroncular stenosis [9]. However, they didn't find a cutoff point excluding the presence of significant CAD in this category of patients. This population was clearly different from the one we studied including patients with at least two cardiovascular risk factors.

CONCLUSION

CS < 40 excludes significant CAD in asymptomatic high cardiovascular risk population, implying that no further investigations are needed. A simple follow-up can be conducted. A CS = 0 is strongly correlated with normal coronaries. A CS ≥ 40 in this population needs further work-up to confirm the presence or absence of significant CAD.

REFERENCES

1. Matta A, Moussallem N. Evolution of the prevalence of angiographically significant coronary artery disease in Lebanese population referred to cardiac catheterization, *Lebanese Medical Journal* 2017; 65 (4): 205-7.
2. Youssef G, Budoff MJ. Coronary artery calcium scoring, what is answered and what questions remain. *Cardiovasc Diagn Ther* 2012 Jun; 2 (2): 94-105.
3. Sarwar A, Shaw LJ, Shapiro MD et al. Diagnostic and prognostic value of absence of coronary artery calcification. *JACC Cardiovasc Imaging* 2009; 2 (6): 675-88.
4. Shah NR, Coulter SA. An evidence-based guide for coronary calcium scoring in asymptomatic patients without coronary heart disease. *Texas Heart Institute Journal* 2012; 39 (2): 240-2.
5. Iwasaki K. Prevalence of noncalcified coronary plaque on 64-slice computed tomography in asymptomatic patients with zero and low coronary artery calcium. *Can J Cardiol* 2010; 26 (7): 377-80.
6. Villines TC, Hulten EA, Shaw LJ et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) Registry. *J Am Coll Cardiol* 2011; 58: 2533-40.
7. Sarwar A. Diagnostic and prognostic value of absence of coronary artery calcification. *JACC* 2009; 2 (6): 675-88.
8. Bielak L, Rumberger JA, Sheedy PF, Schwartz RS, Peyser PA. Probabilistic model for prediction of angiographically defined obstructive coronary artery disease using electron beam computed tomography calcium score strata. *Circulation* 2000; 102: 380-5.
9. Dupuy O, Hauret L, Bonnevie L et al. Input of coronary artery calcium score assessed by computed tomography in the screening of diabetic coronaropathy, *Diabetes & Metabolism* 2002 ; 28 : 421-5.