

Computerized Tomography (CT) Liver Attenuation Index Versus Coronary Calcium Score as Predictors of Coronary Artery Diseases among patients examined with Coronary Computed Tomographic Angiography

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Article

Summary

Liver attenuation index (LAI) used as a predictor of hepatic steatosis. Several previous studies and literatures tried to correlate between steatosis and coronary artery disease, hence we aimed to evaluate validity of liver attenuation indexas a predictor of coronary artery disease compared to coronary calcium score. We conducted a cross-sectional study included 100 adult patients who met the inclusion criteria and referred to the multi detector computed tomographic unit in faculty of medicine \ Kufa university \ Iraq, between July 2019 to end of January 2020. Calcium score and LAI are measured in unenhanced study and we compared the results with the coronary computed tomographic angiographic findings. Our data analysis revealed that revealed 21 steatotic patients, 41patients with calcification was more frequentin steatotic than non-steatotic cases, 4.6% and 39.2%, respectively. Liver attenuation index showed low sensitivity (44%),fair specificity of (62%), low accuracy (58%), in prediction of significant angiographic findings. CAC score a .8%sensitivity, 89% specificity and 84% accuracy (84%). In conclusion Liver attenuation index had no significant prediction of coronary artery disease. Coronary calcium score was a good predictor of coronary artery disease. So we recommend continue using coronary calcium score in assessment of patients with coronary artery disease.

Keywords: Coronary artery disease, steatosis, computerized tomography, coronary calcium score, liver attenuation index

1. INTRODUCTION

Coronary artery disease (CAD) is one of the most frequent health problem and kills many people (1,2). Multiple factors are linked to increased incidence of atherosclerotic heart diseases, these factors can be categorized as non-modifiable risk factors such as age, gender, ethnicity, genetic predisposition and family history of CAD. Modifiable risk factors contribute to CAD include hypertension, diabetes mellitus, smoking, alcohol consumption, besity/overweight, poor diet and nutrition, physical inactivity, stress, microalbuminurea and atherogenic dyslipidemia (3)

Diagnosis of Coronary Artery Disease based on clinical features, history and investigations such as Electrocardiogram, Echocardiogram (ECHO) and stress Echocardiogram, Stress Thallium Test, Coronary computed tomographic angiography (CCTA) remains the gold standard in the diagnosis of coronary artery disease, it has increasingly become a viable noninvasive alternative. Studies assessing the diagnostic performance of CCTA have typically compared its ability to detect significant coronary lesions (blockage of greater than 50%) versus lesions discovered in those same patients on subsequent invasive coronary angiography (4–8). Prediction and diagnosing CAD have a great concerns among clinicians, cardiologists as well as radiologists. Previous literatures and studies investigates the role of different tools for prediction of CAD, one of these indices is calcium score (CAC score) (9,10). Hepatic attenuation index or liver attenuation index (LAI) used as a predictor of hepatic steatosis and several previous studies and literatures tried to correlate between steatosis and CAD (11-16). Coronary artery calcium score (CAC score) is a test that measures the amount of calcium in the walls of the heart's arteries. Coronary calcium scan is one way to estimate someone's risk of developing heart disease or having a heart attack or stroke(1.). Multidetector computed tomography (MDCT) angiography is a predictive tool for (CAD) (6). Fatty liver disease comprises a spectrum of conditions (simple hepatic steatosis, steatohepatitis with inflammatory changes, and end-stage liver disease with fibrosis and cirrhosis). Diffuse steatosis reduces liver attenuation. On non-contrast CT, moderate to severe steatosis (at least 30% fat fraction) is predicted relative hypo attenuation (liver attenuation lower than 10 HU less than that of spleen), absolute low attenuation: liver attenuation lower than 40 HU (18–20), liver-to-spleen attenuation ratio less than 1 (21). In comparison, contrast enhanced CT is poorly predictive of steatosis. Nevertheless, some

criteria for diffuse hepatic steatosis on contrast enhanced CT have been propose (20). Liver attenuation index (LAI) is derived and defined as the difference between mean hepatic and mean splenic attenuation. The LAI greater than 5 HU correlated with macro vesicular steatosis of <5%. The LAI between -10 and 5 HU correlated well with macro vesicular steatosis in the mild-to-moderate range of 6%–30%. The LAI of less than -10 HU correctly predicted four of four donor livers with greater than 30% macro vesicular steatosis (22–24)

2. PATIENTS and METHODS

A cross sectional study conducted at multi detector CT unit in Faculty of Medicine \ Kufa university during the period from July 2019 to end of January 2020. A total of 120 adult Iraqi patients with chest pain and clinical criteria of CAD undergoing CAC score and coronary CT angiography were included. Patient with any absolute or relative contraindication to CCTA, performed special interventional cardiac procedures , alcoholic or with chronic liver diseases were excluded from the study, however, twenty patients were excluded

Data were collected using a pre constructed data collecting sheet, included demographic and clinical variables

Calcium score was measured as the total and detailed measurements including the major 3 vessels: 1. Right coronary artery (RCA), 2.Left anterior descending artery (LADA) and 3.Left circumflex artery(LCXA).

The total Agatston score (AS) was calculated by summation of every calcific focus in all above mentioned coronary arteries .

According to CAC score that based on first Rumberger guidelines they were sub grouped as following: no calcium (0 CAC score) and with calcium (≥ 1)

After assessment of patients with CTCA, the following findings were searched for: 1.normal 2. Non-significant stenosis (less than 50 %) in each one of the three vessels and 3.significant stenosis (more than 50 %) in each one of three vessels and according to these findings, the patients were categorized into:

- 1. Patients with CAD , including both with significant stenosis (more than $50\,\%$) and non-significant (less than $50\,\%$ stenosis) .
- 2. Patients with negative findings assigned as Non CAD patients .

Liver attenuation index (LAI) was estimated by measuring density of visualized parts of liver and spleen by measuring at least 5 region of interest and then mean value was considered as hepatic or splenic density and then calculated according to equation of : LAI = mean density of liver in Hounsfield unit (HU) - mean density of spleen in (HU) The examinations were done at spiral CT unit in faculity of medicine Kufa university by Siemens computed tomography (Somatom definition edge -256 slice) which is made in Germany. Section thickness of 0.625 mm was obtained with Gantry rotation of 350–500 msec).

Data were entered and analyzed using the statistical package for social sciences (SPSS) version 25. Appropriate statistical tests and procedures were applied accordingly at a level of significance (P value) of less than or equal to 0.05 considered significant.

3. RESULTS

Among the studied group, 21(21%) were steatotic and the remaining .9 were not, onthe other hand, calcification (calcium score ≥ 1) was reported in 41 cases (41%) while 59 (59%) of the cases had no calcification, (Table 1).

Ten steatotic patients (4..6%) and 31 non-steatotic patients (39.2%) had calcification, indicated more frequent calcification in steatotic cases, however, the difference did not reach the statistical significance, (P. value > 0.05), (Table 2) Furthermore, the distribution of angiographic findings across the steatosis status revealedno statistical significant differences in the distribution of angiographic findings among steatotic and non-steatotic cases, (P. value > 0.05), moreover, the validity of Liver attenuation significant angiographic findings revealed low sensitivity index in prediction of (44%), fair specificity of (62%), low accuracy (58%), poor positive predictive value (PPV) (23%) and good negative predictive value (NPV) (80%). In prediction of insignificant angiographic findings, steatosis had low sensitivity (36%), fair specificity and accuracy of (66%) and (60%), respectively, while poor PPV (21%), and good NPV (80%). When the validity assessed using total abnormal angiographic findings (significant and insignificant) as one group vs. normal findings, the validity was not much different, but a relative increase in the sensitivity (63%), specificity was 48%, accuracy 51%, PPV was 22% and NPV was 85%, (Table 3).

Regarding the relationship between calcification and angiographic findings (Figure 3), it had been significantly found that significant angiographic findings were more frequent, 23/41~(56.1%), among cases with calcification compared to only ./59 (11.9%) of those with no calcification, also insignificant findings were more frequent in this subgroup than those with no calcification, (P = 0.001). From other point of view, CAC score had good sensitivity (.8%), specificity (89%), and accuracy (84%), PPV (83%) and NPV (85%), in prediction of significant angiographic findings, lower validity parameters were reported in prediction of insignificant findings or total abnormal findings, (Table 4).

Further analysis was performed using Z statistics to compare the validity of Liver attenuation index vs. CAC score in prediction of angiographic findings, this analysis revealed that calcification had significantly higher validity parameters in prediction of significant and insignificant angiographic findings, however, the difference in specificity accuracy and NPV of prediction of insignificant findings were statistically insignificant, (P>0.05), (Table 5).

No significant association between history of hypertension and Steatosis was found (P>0.05). Conversely, hypertension was significantly associated with the presence of calcification (P. value = 0.008) and Significant angiographic findings (P. value = 0.014), where calcification was more frequent among hypertensive patients, (58.3%) compared to 31.3% among non-hypertensive. Abnormal angiographic findings was significantly more frequent in hypertensive patients compared to non-hypertensive, insignificant stenosis found in 38.9% of hypertensive and 15.6% of non-hypertensive. Significant stenosis foundin 4..2% compared to 20.3% among hypertensive and non-hypertensive, respectively, (P.value = 0.001), (Table 6).

The relationship between Diabetes mellitus was significant with Steatosis, calcification and abnormal angiographic findings, in all comparison, (P. value<0.05), (Table.). Similarly, Hyperlipidemia was significantly associated with each of Steatosis, calcification and abnormal angiographic findings, in all comparison, (P. value<0.05), (Table 8).

Steatosis was more frequent in smokers (35..%) compared to non-smokers (18.6%),however, the difference did not reach the statistical significance, (P>0.05). Calcification was significantly more frequent among smokers, (69.6%) compared to 32.3%.5 among none

smokers, (P. value = 0.02.), indicated a significant association. Another significant association was found between smoking and abnormal angiographic findings where these findings were more frequent among smoker, compared to non-smoker, ,(P. value =0.006), (Table 9).

As it shown in (Table 10), obese patients were more likely to be steatotic than non-obese, where 53.1% of obese were steatotic compared to only 5.9% among non-obese (P. value = 0.001). Additionally, calcification and abnormal angiographic findings were significantly associated with obesity, (P<0.05).

Table 1. Distribution of Steatosis and Calcification of the studied group

	Variable	No.	%
Ctantonia	Yes	21	21.0
Steatosis	No	.9	.9.0
Calcification	Yes	41	41.0
Calcium score ≥ 1	No	59	59.0

Table 2 Distribution of calcification among steatotic and non-steatotic patients

Calcification	Stea	totic	Non St	teatotic		
Calcification	No.	%	No.	%		
Yes	10	46	31	39.2		
No	11	52.4	48	60.8		
Total	21	100.0	.9	100.0		
P. value; 0.488 not significant						

Table 3. Distribution of angiographic findings among steatotic and non-steatotic patients and the validity of LAI in prediction of angiographic findings

An air annulair fin din a	Ste	atotic	Non Stea	ntotic
Angiographic finding	No.	%	No.	%
Normal*	9	42.9	3.	46.8
Insignificant	5	23.8	19	24.1
Significant	•	33.3	23	29.1
Total	21	100	.9	100
Validity parameter	An			
vanuity parameter	Significant	Insignificant	Abnormal	
SENSITIVITY	44.0%	36.0%	63%	
Specificity	62.0%	66.0%	48%	
Accuracy	58.0%	60.0%	51%	
PPV	23.0%	21.0%	22%	
NPV	80.0%	80.0%	85%	

^{*}normal subgroup used as reference group,

P. value > 0.05, not significant,

PPV: positive predictive value, NPV: negative predictive value, Abnormal: abnormal angiographic findings (significant and insignificant)

Table 4. Distribution of angiographic findings among patients with and without calcification and the validity of calcification in prediction of angiographic findings

Ancie anombie fin din a	Calci	fication	No Calcification		
Angiographic finding	No.	%	No.	%	
Normal		. 17.1		66.1	
Insignificant	11	26.8	13	22.0	
Significant	23	56.1		11.9	
Total	41	100.0	59	100.0	
Volidity nonomotor	Angiogra	phic finding			
Validity parameter	Significant	Insignificant	Abnormal		
Sensitivity	.8%	56%	83%		
Specificity	89%	.2%	66%		
Accuracy	84%	69%	.3%		
PPV	83%	38%	63%		
NPV	85%	85%	85%		

^{*}normal subgroup used as reference group,

P. value < 0.05 significant,

PPV: positive predictive value, NPV: negative predictive value, Abnormal: abnormal angiographic findings (significant and insignificant)

Table 5. Comparison of validity parameters of Steatosis and Calcification in prediction of significant, insignificant and abnormal angiographic findings

	Validity		Angiographic findi	ng
INDEX	parameter	Significant	Insignificant	Abnormal
	Sensitivity	44%	36%	63%
Steatosis	Specificity	62%	66%	48%
	Accuracy	58%	60%	51%
	PPV	23%	21%	22%
	NPV	80%	80%	85%
	Sensitivity	.8%	56%	83%
	Specificity	89%	.2%	66%
Calcification	Accuracy	84%	69%	.3%
	PPV	83%	38%	63%
	NPV	85%	85%	85%
P. values				
P1 (compare sensitivi	ity)	0.001 sig	0.00. sig	0.002 sig
P2 (compare Specificity)		0.001 sig	0.445 ns	0.015 sig
P3 (compare Accuracy)		0.001 sig 0.23. ns		0.002 sig
P4 (compare PPV)		0.001 sig	0.013 sig	0.001 sig
P5 (compare NPV)		0.45. ns	0.45. ns	0.843 ns

sig: significant, ns: not significant, z test used to compare rates

Table 6. Relationship of hypertension with Steatosis, Calcification and Angiographic findings of the studied group

Parameter						
		Y	es	No		P. value
		No.	%	No.	%	
Staatogic (n=21)	Steatotic	5	13.9	16	25.0	0.190 ns
Steatosis (n=21)	Non Steatotic	31	86.1	48	.5.0	
Calcification	Yes	21	58.3	20	31.3	0.008
(n=41)	No	15	41	44	68.8	sig
	Normal	5	13.9	41	64.1	
Angiographic finding	Insignificant	14	38.9	10	15.6	0.001 sig
	Significant	1.	42	13	20.3	318

Table Relationship of Diabetes with Steatosis , Calcification and Angiographic findings of the studied group

Parameter			Diabetes				
		Yes		No		P. value	
		No.	%	No.	%		
Stantonia	Steatotic	12	44.4	9	12.3	0.001	
Steatosis	Non Steatotic	15	55.6	64	8	sig	
Coloification	Yes	1.	63.0	24	32.9	0.012	
Calcification	No	10	30	49	61	sig	
	Normal	4	14.8	42	55		
Angiographic finding	Insignificant	11	40	13	18	0.001 sig	
	Significant	12	44.4	18	24] -18	

Table 8. Relationship of Hyperlipidemia with Steatosis, Calcification and Angiographic findings of the studied group

		Hyperlipidemia				
		Yes		No		P. value
		No.	%	No.	%	•
	Steatotic	9	39.1	12	15.6	0.032
Steatosis	Non Steatotic	14	60.9	65	84.4	sig
	Total	23	100.0		. 100.0	
	Yes	16	69.6	25	32.5	0.033
Calcification	No		30.4	52	65	sig
	Total	23	100.0	••••	. 100.0	
	Normal	4	14%	42	54.5%	
Angiographic finding	Insignificant	8	34.8%	16	20.8%	0.00
	Significant	11	48%	19	24%	sig
	Total	23	100.0		. 100.0	

Table 9. Relationship of Smoking with Steatosis, Calcification and Angiographic findings of the studied group

	<u> </u>						
			Smoking				
		Y	Yes		No		
		No.	%	No.	%		
Steatosis	Steatotic	5	35	16	18.6	0.145	
Steatosis	Non Steatotic	9	64.3	.0	81.4	ns	
Coloification	Yes	10	.1.4	31	36.0	0.02	
Calcification	No	4	28.6	55	64.0] <u>.</u> .	
	Normal	1	1	45	52.3	sig	
Angiographic finding	Insignificant	5	35	19	22.1	0.006 sig	
	Significant	8	51	22	25.6	515	

Table 10. Relationship of Obesity with Steatosis, Calcification and Angiographic findings of the studied group

Parameter						
		Obese		Non-obese		P. value
		No.	%	No.	%	
Steatosis	Steatotic	1.	53.1	4	5.9	0.001
Steatosis	Non Steatotic	15	46.9	64	94.1	sig
Calcification	Yes	19	59.4	22	32.4	0.019
Calcification	No	13	40.6	46	66	sig
	Normal		21.8	39	54	
Angiographic finding	Insignificant	11	34.4	13	19.1	0.004 sig
	Significant	14	43.8	16	23.5	

4. DISCUSSION

The present study assessed the value of LAI in prediction of CAD among group of Iraqi patients who performed CCTA. Liver attenuation index validity was assessed against the angiographic findings and further compared to CAC score. Among the studied group, (21%) were steatotic while calcification (calcium score ≥ 1) was reported in 41 cases. The distribution of calcification across steatosis, revealed that 10 steatotic patients (4..6%),31 non-steatotic cases (39.2%) had calcification, which indicated more frequent calcification in steatotic cases, however, the difference did not reach the statistical significance, (P. value > 0.05). Furthermore, the distribution of angiographic findings across the steatosis status revealed no statistical significant differences in the distribution angiographic findings among steatotic and non-steatotic (P. value > 0.05), moreover, the validity of steatosis index in prediction of significant angiographic findings revealed low sensitivity (44%), fair specificity of (62%), low accuracy (58%), poor PPV (23%) and good NPV (80%). In prediction of insignificant angiographic findings, steatosis had low sensitivity (36%), fair specificity and accuracy of (66%) and (60%), respectively, while poor PPV (21%), and good NPV (80%). When the validity assessed using total abnormal angiographic

findings (significant and insignificant) as one group vs. normal findings, the validity was not much different, but a relative increase in the sensitivity (63%), specificity was 48%, accuracy 51%, PPV was 22% and NPV was 85%. The current study found that calcification had significantly higher validity parameters in prediction of significant and insignificant findings, however, the difference in specificity accuracy and NPV of angiographic prediction of insignificant findings were statistically insignificant, (P>0.05). The following studies are consistent with our study as Perry, et al said that steatosis was a biomarker for subsequent CAD but not an independent risk factor (25). A previous study concluded that NAFLD is less likely to be a direct mediator of subclinical CAD and instead of that may be regarded as (Epiphenomena) (26). Kathleen Jacobe and Shron Brouha found no obvious correlation between CAD and steatosis and the visceral adiposity can be used as a risk factor for coronary heart disease (2.). Nazim Ghouri, David Preiss et al who found that they conclude that a diagnosis of steatosis (or elevated liver enzymes) is insufficient to warrant labeling patients as being at high risk for CAD. And conversely ,the evidence of NAFLD should be an indication for screening for DM. Theevidence for CAD risk screening based on the presence of hepatic steatosis is weaker and they recommend that assessment of risks is determined according to measurement of established risk factors using existing charts (28) .Rashmee Patil and Gagan K howed that steatotic patients may get benefit from more careful surveillance and early management. But, despite evidence linking increased CAD risk with NAFLD, there is still uncertainty about the prognostic role of hepatic steatosis in risk stratification for CAD ad suggest Additional, follow-up studies are advised to assess if steatosis can be added as risk scoring predictor. And Furthermore, the question is whether there is a prognostic value of steatosis in the development and progression of CAD (29). P.Loria and A. Lonardo et al also agreed that there is a relationship between steatosis and CAD clinically and epidemiologically but further studies need to be done to confirm that significantly (30). Cadematiri & Sverzellati et al found in a study done at 2016 that there is no standardized approach to measure liver fatty tissues in computed tomography because there are many parameters and different strategies that may affect quantifications (31). Wai-Sun Wong & Wong et al conclude that steatosis cannot predict mortality and morbidity in patients with established coronary artery disease (32) .Tantawy & Ali et al. said that there is significant association between

hepatic steatosis & atherosclerosis (insignificant CAD) but no significant correlation between NAFLD and significant CAD, so they suggest that NAFLD may be used as a predictor for insignificant CAD not for significant one (16). Targher & Arcaro et al in previous study also agreed that NAFLD patients may developed subclinical CAD when compared with Non steatotic one (33). Rajiv Chabra and O'Keefe (in study done at 2013) correlated between steatosis as an independent risk factor for increasing CAC score but agree that steatosis as an independent predictor for CAD need to be further studied (34). Ling, SUN; Shu-zheng, LÜ in a previous cross sectional study, also suggested that steatosis is associated with coronary heart disease, in addition to the known risk factors, but they could not assure that NAFLD is an independent risk factor or epiphenomenon of CAD (35).

Conversely the following studies disagree with our study in different points as following: Mustafa Koplay & Mustafa Gok et al. found in study done at 2019 Using MRI ,CT and ultrasonography that NAFLD as part of metabolic syndromes is associated with increased risk of CAD and it might be not only a marker but also an early mediator for coronary heart disease (36). Dae Hee Choi, Sung Joon Lee et al in a study done in Korea at 2013 suggested that cases of CAD proved by CCTA is strongly correlated with steatosis (by ultrasonography), and NAFLD is a significant predictor of coronary heart disease (3.) .Mary F.Feitosa and Alexander P.Reiner et al (in study done at 2013) said that they found hepatic steatosis is a predictor of CAD independent on other risk factors. The study was done using CT and ALT level (38). Donghee Kim & Su Yeon Choi et al. found that patients with NAFLD will show increased risk of coronary artery disease . A group of patients with steatosis shows increase in CAC score more than 100. Additionally NAFLD might be regarded as an independent risk factor for CAD (39). Wolff & Daniel Bos et al (study at 2016) also found that high amount of steatosis is related to larger volumes of epicardial fat and CAC score independent of CAD risk factors providing an promising novel about role of liver as a marker of vascular disease (40).

We can explain this discrepancy in that different tools are used to evaluate the amount of fatty steatosis including ultrasonography, MRI, CT and biochemical markers, different cut off points for the definition of steatosis, a relatively small sample of general population taken in our study with short period in comparison with large sample and long period of

other studies and some studies choose a selected patients with steatosis.

From other point of view, in the present study, steatosis and Calcification were more frequent in smokers compared to non-smokers. Additionally, smoking was significantly associated with abnormal angiography findings. Hyperlipidemia also as another risk factor for CAD was found in 23 % of the studied sample in this study which was lower than expected among Iraqi population (41), while it approximate the prevalence recorded in neighbor countries according to the same study (10-23 %).

Hyperlipidemia was significantly associated with each of steatosis, calcification and abnormal angiographic findings. The relationship between Diabetes mellitus was significant with steatosis, calcification and abnormal angiographic findings. No significant association between history of hypertension and Steatosis. Conversely, hypertension was significantly associated with the presence of calcification and Significant angiographic findings. Abnormal angiographic findings was significantly more frequent in hypertensive patients compared to non-hypertensive, insignificant stenosis. Our findings regarding the demographic factors agreed many previous studies (42-50)

Regarding the descriptive statistics of the studied parameters; CAC score showed a wide range of variation (0-2286) with a mean of 121, this variation attributed to degree of calcification particularly the angiographic findings revealed that 30% patients were found to have significant stenosis that attributed to plaque formation and calcification of arteries. Regarding the relationship between calcification and angiographic findings, it had been significantly found that significant angiographic findings were more frequent, 23/41 (56.1%), among cases with calcification compared to only ./59 (11.9%) of those with no calcification, also insignificant findings were more frequent in this subgroup than those with no calcification, (P = 0.001). From other point of view, CAC score had good sensitivity (.8%), specificity (89%), and accuracy (84%), PPV (83%) and NPV (85%), in prediction of significant angiographic findings, lower validity parameters were reported in prediction of insignificant findings or total abnormal findings. The following studies are found to be consistent with our study as following: Shabestari et al. who agree that CAC score is accepted as a standard reference for detection of risk of subsequent heart attacks (51) K.N.Zhuravlev & V.E.Sinitsyn et al. who found that CAC score should be regarded as a strong screening method for CAD (52). Mark .J.Pletcher and Jeffrey A.Tice et al in

addition to Geluk & Dikkers who found in a previous studies that CAC score is an independent predictor for coronary heart problems (53) and is a suitable initial noninvasive procedure in asymptomatic patients . S.Leschka & H.Scheffel et al who said that combination of CAC score & CCTA with increase the specificity without affecting the sensitivity of diagnosing CAD (54). Christopher Herzog and Martina Britten et al said that Calcium scoring as a single method showed highest sensitivity in the detection of

coronary atherosclerosis and combination with MD CTA helped to distinctly increase

specificity and NPV (55). George T. Lau, Lloyd J. Ridley et al agreed that A calcium

score can be used to potentially identify patients with significant coronary stenoses not

detected at CT angiography (56).

Maeda & Yamamoto et al found in study done in Japan in 2016 agreed that both measures are also significantly correlated as a predictor and diagnostic measures respectively (5.) Kazuhiro Osawa and Toru Miyoshi et al found that, the prevalence of DM in patients with NAFLD was significantly higher than that in patients who did not have NAFLD (58). The liver attenuation index in the prevalent study ranged from (-10)-(33) and according to standard cut points of steatosis which was in our study depending on absolute low attenuation: liver attenuation lower than 40 HU (20, 59), liver-to-spleen

attenuation ratio less than 1 (21, 60)

5. CONCLUSIONS

Liver attenuation index had no significant prediction of coronary artery disease. Coronary calcium score was a good predictor of coronary artery disease. So we recommend continue

using coronary calcium score in assessment of patients with coronary artery disease.

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical principles for medical research involving human subjects. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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References

- 1. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016 Jul;4(13):256–64.
- 2. Samani NJ, Erdmann J, Hall AS, Hengstenberg C, Mangino M, Mayer B, Dixon RJ, Meitinger T, Braund P, Wichmann HE BJ. Genomewide association analysis of coronary artery disease. N Engl J Med. 200.;35.(5):443–53.
- 3. Huma S, Tariq R, Amin F, Mahmood KT. Modifiable and non-modifiable predisposing risk factors of myocardial infarction-A review. Journal of pharmaceutical sciences and research. 2012;4(1):1649-5..
- 4. Alizadehsani R, Habibi J, Hosseini MJ, Mashayekhi H, Boghrati R, Ghandeharioun A, Bahadorian B, Sani ZA. A data mining approach for diagnosis of coronary artery disease. Computer methods and programs in biomedicine. 2013 Jul 1;111(1):52-61.
- 5. Genders TS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, Galema TW, Meijboom WB, Mollet NR, de Feyter PJ, Cademartiri F. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. European.
- 6. de Graaf FR, Schuijf JD, van Velzen JE, Kroft LJ, de Roos A, Reiber JH, Boersma E, Schalij MJ, Spanó F, Jukema JW, van der Wall EE. Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of sig.
- 7. Chen GB, Wu H, He XJ, Huang JX, Yu D, Xu WY, Yu H. Adenosine stress thallium-201 myocardial perfusion imaging for detecting coronary artery disease at an early stage. Journal of X-ray science and technology. 2013 Jan 1;21(2):31.-22.
- 8. Chang HJ, Chung N. Clinical perspective of coronary computed tomographic angiography in diagnosis of coronary artery disease. Circulation Journal. 2011;.5(2):246-52.
- 9. Wolterink JM, Leiner T, de Vos BD, van Hamersvelt RW, Viergever MA, Išgum I. Automatic coronary artery calcium scoring in cardiac CT angiography using paired convolutional neural networks. Med Image Anal. 2016;34:123–36.
- 10. de Vos BD, Wolterink JM, Leiner T, de Jong PA, Lessmann N, Išgum I. Direct automatic coronary calcium scoring in cardiac and chest CT. IEEE Trans Med Imaging. 2019;38(9):212.–38.

- 11. Limanond P, Raman SS, Lassman C, Sayre J, Ghobrial RM, Busuttil RW, et al. Macrovesicular Hepatic Steatosis in Living Related Liver Donors: Correlation between CT and Histologic Findings. Vol. 230, Radiology. 2004. p. 2.6–80.
- 12. Hahn L, Reeder SB, del Rio AM, Pickhardt PJ. Longitudinal changes in liver fat content in asymptomatic adults: hepatic attenuation on unenhanced CT as an imaging biomarker for steatosis. Am J Roentgenol. 2015;205(6):116.—.2.
- 13. Park HE, Kwak M-S, Kim D, Kim M-K, Cha M, Choi S-Y. Nonalcoholic fatty liver disease is associated with coronary artery calcification development: a longitudinal study. J Clin Endocrinol Metab. 2016;101(8):3134–43.
- 14. Filippo Cademartiri, Nicola Sverzellati, Andrea I. Guaricci, Erica Maffei, Fat and cardiovascular risk: the role of Cardiac CT, European Heart Journal Cardiovascular Imaging. 2016;1.(12):1368–9.
- 15. Lee MK, Park HJ, Jeon WS, Park SE, Park CY, Lee WY, et al. Higher association of coronary artery calcification with non-alcoholic fatty liver disease than with abdominal obesity in middle-aged Korean men: The Kangbuk Samsung Health Study. Cardiovasc Diabetol. 2015;14(1):1–9.
- 16. Tantawy WH, Ali KM, Aziz SF. Evaluation of Coronary Artery Disease among Population with Fatty Liver Disease Using Multi-Slice Computed Tomography. Egypt J Hosp Med. 2018;.2(1):120–9.
- 17. Mohammad AM, Jehangeer HI, Shaikhow SK. Prevalence and risk factors of premature coronary artery disease in patients undergoing coronary angiography in Kurdistan, Iraq. BMC Cardiovasc Disord. 2015 Nov 18;15:155.
- 18. Ma X, Holalkere NS, Mino-Kenudson M, Hahn PF, Sahani DV. Imaging-based quantification of hepatic fat: methods and clinical applications. Radiographics. 2009 Sep;29(5):1253-...
- 19. Boyce CJ, Pickhardt PJ, Kim DH, Taylor AJ, Winter TC, Bruce RJ, Lindstrom MJ, Hinshaw JL. Hepatic steatosis (fatty liver disease) in asymptomatic adults identified by unenhanced low-dose CT. American Journal of Roentgenology. 2010 Mar;194(3):623-8.
- 20. Frank Gaillard. Diffuse hepatic steatosis / Radiology Reference Article/Radiopaedia.org.13\13Available-from https://radiopaedia.org/articles/diffusehepaticsteatosis.

- 21. Wells MM, Li Z, Addeman B, McKenzie CA, Mujoomdar A, Beaton M, Bird J. Computed tomography measurement of hepatic steatosis: prevalence of hepatic steatosis in a Canadian population. Canadian Journal of Gastroenterology and Hepatology. 2016 Jan 1;2016.
- 22. Lee SW, Park SH, Kim KW, Choi EK, Shin YM, Kim PN, et al. Unenhanced CT for assessment of macrovesicular hepatic steatosis in living liver donors: comparison of visual grading with liver attenuation index. Radiology. 200.;244(2):4.9–85.
- 23. Gupta V, Pallavi CJ, Kalyanpur A, Dayananda L. Multi-detector CT in the pre-operative assessment of live donors for liver transplantation. International Surgery Journal. 201.;4(6):1930–5.
- 24. Karakas HM, Kirimlioglu H, Kahraman B, Yilmaz S, Kirimlioglu V. The Assessment of Hepatosteatosis in Living-Donor Liver Transplant: Comparison of Liver Attenuation Index and Histopathologic Results. Exp Clin Transplant Off J Middle East Soc Organ Transplantation. 2015;15(1):69—...
- 25. PJ Pickhardt, L Hahn, AM del Rio. Natural history of hepatic steatosis: observed outcomes for subsequent liver and cardiovascular complications. American Journal of Roentgenology, 2014, 202.4: .52-.58.
- 26. RL McKimmie, KR Daniel, JJ Carr. Hepatic steatosis and subclinical cardiovascular disease in a cohort enriched for type 2 diabetes: the Diabetes Heart Study. The American journal of gastroenterology, 2008, 103.12: 3029.
- 27. K Jacobs, S Brouha, R Bettencourt. Association of nonalcoholic fatty liver disease with visceral adiposity but not coronary artery calcification in the elderly. Clinical Gastroenterology and Hepatology, 2016, 14.9: 133.-1344. e3.
- 28. GHOURI, Nazim; PREISS, David; SATTAR, Naveed. Liver enzymes, nonalcoholic fatty liver disease, and incident cardiovascular disease: a narrative review and clinical perspective of prospective data. Hepatology, 2010, 52.3: 1156-1161.
- 29PATIL, Rashmee; SOOD, Gagan K. Non-alcoholic fatty liver disease and cardiovascular risk. World journal of gastrointestinal pathophysiology, 201., 8.2: 51.
- 30. P Loria, A Lonardo, S Bellentani, CP Day. Non-alcoholic fatty liver disease (NAFLD) and cardiovascular disease: an open question. Nutrition, Metabolism and Cardiovascular Diseases, 200., 1..9: 684-698.

- 31. F Cademartiri, N Sverzellati, AI Guaricci, E Maffei. Fat and cardiovascular risk: the role of Cardiac CT. 2016.
- 32. VWS Wong, GLH Wong, GWK Yip, AOS Lo. Coronary artery disease and cardiovascular outcomes in patients with non-alcoholic fatty liver disease. Gut, 2011, 60.12: 1721-1727.
- 33. G Targher, A Mantovani, I Pichiri, L Mingolla. Nonalcoholic fatty liver disease is independently associated with an increased incidence of cardiovascular events in type 2 diabetic patients. Diabetes care, 2007, 30.8: 2119-2121.
- 34. R Chhabra, JH O'Keefe, H Patil, E O'Keefe. Association of coronary artery calcification with hepatic steatosis in asymptomatic individuals. In: Mayo Clinic Proceedings. Elsevier, 2013. p. 1259-1265.
- 35. LING, Sun; SHU-ZHENG, L. Ü. Association between non-alcoholic fatty liver disease and coronary artery disease severity. Chinese medical journal, 2011, 124.6: 867-872.
- 36. KOPLAY, Mustafa; GOK, Mustafa; SIVRI, Mesut. The association between coronary artery disease and nonalcoholic fatty liver disease and noninvasive imaging methods. Electronic Journal of General Medicine, 2019, 16.6.
- 37. DH Choi, SJ Lee, CD Kang, MO Park. Nonalcoholic fatty liver disease is associated with coronary artery disease in Koreans. World Journal of Gastroenterology: WJG, 2013, 19.38: 6453.
- 38. MF Feitosa, AP Reiner, MK Wojczynski, M Graff. Sex-influenced association of nonalcoholic fatty liver disease with coronary heart disease. Atherosclerosis, 2013, 227.2: 420-424.
- 39. D Kim, SY Choi, EH Park, W Lee, JH Kang, W Kim. Nonalcoholic fatty liver disease is associated with coronary artery calcification. Hepatology, 2012, 56.2: 605-613.
- 40. L Wolff, D Bos, SD Murad, OH Franco. Liver fat is related to cardiovascular risk factors and subclinical vascular disease: the Rotterdam Study. European Journal of Echocardiography, 2016, 17.12: 1361-1367.
- 41. MULA-ABED, W.; CHILMERAN, Saba K. Prevalence of dyslipidemia in the Iraqi adult population. Saudi medical journal, 2007, 28.12: 1868.
- 42. PM Gholam, L Flancbaum, JT Machan. Nonalcoholic fatty liver disease in severely obese subjects. American Journal of Gastroenterology, 2007, 102.2: 399-408.
- 43. Dixon, John B.; BHATHAL, Prithi S.; O'BRIEN, Paul E. Nonalcoholic fatty liver disease:

- predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology, 2001, 121.1: 91-100.
- 44. SH Kim, GY Cho, I Baik, J Kim, SJ Kim, JB Lee. Association of coronary artery calcification with obstructive sleep apnea and obesity in middle-aged men. Nutrition, Metabolism and Cardiovascular Diseases, 2010, 20.8: 5.5-582.
- 45. Y Chang, BK Kim, KE Yun, J Cho, Y Zhang. Metabolically-healthy obesity and coronary artery calcification. Journal of the American College of Cardiology, 2014, 63.24: 26.9-2686.
- 46. Albrink, Margaret J.; MEIGS, J. Wister; MAN, Evelyn B. Serum lipids, hypertension and coronary artery disease. The American journal of medicine, 1961, 31.1: 4-23.
- 4.. JF Price, PI Mowbray, AJ Lee, A Rumley. Relationship between smoking and cardiovascular risk factors in the development of peripheral arterial disease and coronary artery disease; Edinburgh Artery Study: Edinburgh Artery Study. European heart journal, 1999, 20.5: 344-353.
- 48. AJ Hartz, PN Barboriak, AJ Anderson, RG Hoffmann. Smoking, coronary artery occlusion, and nonfatal myocardial infarction. Jama, 1981, 246.8: 851-853.
- 49. RM Williamson, JF Price, S Glancy, E Perry. Prevalence of and risk factors for hepatic steatosis and nonalcoholic fatty liver disease in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study. Diabetes care, 2011, 34.5: 1139-1144.
- 50. Clark, Jeanne M.; DIEHL, Anna Mae. Hepatic steatosis and type 2 diabetes mellitus. Current diabetes reports, 2002, 2.3: 210-215.
- 51. Shabestari, Abbas Arjmand. Coronary artery calcium score: a review. Iranian Red Crescent Medical Journal, 2013, 15.12.
- 52. Zhuravlev, K. N.; SINITSYN, V. E.; SHPEKTOR, A. V. Coronary Calcium Score as Powerful Screening Method for Cardiovasculsr Dis-eases (Literature Review). Radiology, 2019, 6: .8.
- 53. MJ Pletcher, JA Tice, M Pignone. Using the coronary artery calcium score to predict coronary heart disease events: a systematic review and meta-analysis. Archives of internal medicine, 2004, 164.12: 1285-1292.
- 54. S Leschka, H Scheffel, L Desbiolles, A Plass. Combining dual-source computed tomography coronary angiography and calcium scoring: added value for the assessment

- of coronary artery disease. Heart, 2008, 94.9: 1154-1161.
- 55. C Herzog, M Britten, JO Balzer, MG Mack, S Zangos. Multidetector-row cardiac CT: diagnostic value of calcium scoring and CT coronary angiography in patients with symptomatic, but atypical, chest pain. European radiology, 2004, 14.2: 169-1...
- 56. GT Lau, LJ Ridley, MC Schieb, DB Brieger. Coronary artery stenoses: detection with calcium scoring, CT angiography, and both methods combined. Radiology, 2005, 235.2: 415-422.
- 5.. E Maeda, K Yamamoto, S Kanno, K Ino. Diagnostic phase of calcium scoring scan applied as the center of acquisition window of coronary computed tomography angiography improves image quality in minimal acquisition window scan (Target CTA Mode) using the second generation 320-row CT. The Scientific World Journal, 2016, 2016.
- 58. OSAWA, Kazuhiro, et al. Nonalcoholic hepatic steatosis is a strong predictor of high-risk coronary-artery plaques as determined by multidetector CT. PloS one, 2015, 10.6.
- 59. CJ Boyce, PJ Pickhardt, DH Kim. Hepatic steatosis (fatty liver disease) in asymptomatic adults identified by unenhanced low-dose CT. American Journal of Roentgenology, 2010, 194.3: 623-628.
- 60. OW Hamer, DA Aguirre, G Casola, JE Lavine. Fatty liver: imaging patterns and pitfalls. Radiographics, 2006, 26.6: 163.-1653.