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Original article:

In Hospital Prognostic Value of Hepatic Transaminases in Patients with Acute Coronary Syndrome

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ABSTRACT

Background: The aspartate aminotransferase (AST) alanine aminotransferase (ALT) ratio, previously considered as a serological parameter for identifying the degree of severity of hepatic fibrosis, is also associated with the prognosis of a variety of diseases, including cardiovascular disease. So, this study aimed to evaluate the value of hepatic transaminases as predictors of in hospital mortality and complications in patients that were admitted for acute coronary syndrome.

Patients and Methods: This cross-sectional study was carried out in the Cardiology Department, Faculty of Medicine, Zagazig University and in the Nasser institute for Research and treatment, Egypt on 200 patients with acute coronary syndrome, patients were divided into three groups; unstable angina (13.5%), NSTEMI (14.5%) and STEMI (72%).

Results: There was statistically significant difference in Liver enzymes (AST and ALT) between all groups. Their was significant increase in AST and ALT levels in STEMI group. There was statistically significant increase in Liver enzymes (AST and ALT) in non-survivors group more than in survivors group. There were statistically significant increase in cardiac enzymes (CK-MB and CK), in non-survivors more than in survivors group. There was no statistical significant difference in Alkaline phosphatase in non-survivors more than in survivors group. **Conclusion:** ACS patients had significantly increased hepatic transaminases levels. Moreover, increased risk of in-hospital all-cause mortality was significantly associated with increased levels of hepatic transaminases.

Keywords: Serum Alanine Transaminase, Serum Aspartate Aminotransferase, Acute Coronary Syndrome.

INTRODUCTION

The fundamental liver damage markers blood alanine transaminase (ALT) and serum aspartate amino transferase (AST) are often utilized in clinical practice. A unique blood marker of liver disease, ALT is mostly produced by hepatocytes **(1).**

These enzymes are frequently high in individuals with acute coronary syndromes (ACS) in addition to liver dysfunction, most frequently as a result of myocardial injury but also as a result of inadequate cardiac output and arterial hypoperfusion. AST was the first cardiac biomarker used to help diagnose acute myocardial infarction in 1954, however it is no longer in use due to its lack of specificity for cardiac tissue **(2)**.

Additionally, studies show that elevations in serum transaminases are linked to more severe myocardial injury, systolic dysfunction, and increased cardiac-related mortality in ACS patients if no other causes of liver injury are found **(3).** This study aimed to evaluate the value of hepatic transaminases as predictors of in hospital mortality and complications among those with acute coronary syndrome who are admitted.

PATIENTS AND METHODS

This cross-sectional study was completed at the Zagazig University Faculty of Medicine's Cardiology Department and the Nasser Institute

for Research and Treatment, Egypt. The study was conducted on 200 patients with acute coronary syndrome, patients were divided into three groups: **Group 1:** 27 patients unstable angina, **Group 2:** 29 patients were non STEMI and **Group 3 :** 144 patients were STEMI.

Inclusion criteria: patients with an acute coronary syndrome diagnosis. Every patient included in this study were subjected to coronary angiography ±PCI. **Exclusion criteria**: Patients with elevated transaminases for a variety of conditions other than ACS, such as hepatitis and hepatic cirrhosis, chronic schistosomiasis, hepatobiliary obstructive disease, bone disease, pancreatitis; cardiomyopathy; severe heart failure; severe renal insufficiency; and infectious diseases, were excluded from the study.

All subjects were subjected to full medical history; including past history, comorbidities and analysis of chief complaint. Clinical examination; general examination and emphasizing on chest and cardiac examination. ECHO: LV systolic function, LV diastolic function and complication if present {ventricular septal rupture, acute mitral regurge, ventricular pseudoaneurysm, ventricular aneurysm, LV failure, RV failure, LV mural thrombus and pericarditis}. Coronary angiography ±PCI. CAG was performed via femoral access in all patients.

Electrocardiogram (ECG) on admission. Cardiac enzymes {troponin (T), creatine kinase-MB (CK-MB),CK and LDH}. Liver function tests {Albumin, total protein, total bilirubin, direct bilirubin, AST, ALT, alkaline phosphatase and gamma glutamyl transferase} was obtained at the time of admission. Stool and urine analysis for detection of schistosomiasis eggs. Abdominal ultrasound to detect any liver abnormalities. Renal function tests including urea and creatinin. Lipid profile including LDL, HDL, cholesterol, and triglycerides. Thyroid function tests including T3, T4, and TSH. Coagulation profile PT , aPTT, and INR.

Ethics approval:

The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. Consent from all patient on participating in the study. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Statistical package for Social Science was used to review, code, tabulate, and introduce the acquired data to a computer **(SPSS 25).** Data were presented, and the type of data obtained for each parameter was appropriately analyzed.

Descriptive statistics: Mean, Standard deviation (± SD) whereas Median and Interquartile range (IQR) are used for non-parametric numerical data. and range for parametric numerical data. ***Analytical statistics: Mann Whitney Test (U test)*** was used to evaluate the statistical significance of a difference between two research groups in a non-parametric variable. ***Chi-Square test*** was used to examine the relationship between two qualitative variables. ***Fisher's exact test*** was applied to investigate the association between two qualitative variables when more than 20% of the cells had an expected count of less than 5. P-value: significance level, P>0.05: Non significant (NS), P< 0.05: Significant (S).

RESULTS

The study was conducted on 200 patients with acute coronary syndrome, they were divided into three groups; unstable angina (13.5%), NSTEMI (14.5%) and STEMI (72%). The mean age was 57.79 ± 10.24, Males represented by 86.0% and about 65.0% of patients had past medical history with DM and HTN as shown as table 1.

According to lab investigations, there was significant difference in cardiac enzymes (CK-MB and CK), Liver enzymes (AST and ALT) between all groups, and there was significant difference in lipid profile (total cholesterol, LDL and HDL) between unstable angina Vs. others group and there was significant difference in direct bilirubin between NSTEMI Vs. others. The percentage of patients who had AST ≥2 ULN and ALT ≥2 ULN was significantly increased in STEMI group table 2.

Table 3; showed that there was ***significant decrease*** in EF% in STEMI group other than other groups according to the ECHO findings, while patients in STEMI group had ***significant more*** advanced LV diastolic dysfunction grades. Also in STEMI group, there was ***significant increase*** in percentage of patients who had impaired systolic function and arrhythmias between the three groups, but there was no statistically significant difference in (In hospital mortality).

Table 4; showed that there was no statistical significant difference between two groups in demographics nor past medical history, ***except***

age as there was ***statistical significant increase*** in age within non-survivors group (p-Value <0.05).

Table 5; showed that there was significant increase in cardiac enzymes (CK-MB and CK), total bilirubin, Liver enzymes (AST and ALT), Kidney function (S.creat and urea) and lipid profile (total cholesterol and LDL) in non-survivors other survivors group. Also, there was significant decrease in HDL among non-survivors. The percentage of patients who had AST ≥2 ULN and ALT ≥2 ULN was significant increase in non-survivors group.

Table 6; showed that there was significant decrease in EF% in non-survivors group than survivors group, while patients in non-survivors group had significant more advanced LV diastolic dysfunction grades. Also in non-survivors group, there was significant increase in percentage of patients who had complications (embolic complications, impaired systolic function, RV failure and arrhythmias)

Table 1: Demographic data and risk factors for all the studied groups

		Mean / N	SD / %	Range
Age		57.79	10.24	(25 - 86)
Sex	**Male**	172	86.0%	
	Female	28	14.0%	
BMI		32.53	2.26	(27 - 37)
Smoking		165	82.5%	
DM		130	65.0%	
HTN		131	65.5%	
Diagnosis	**Unstable angina**	27	13.5%	
	NSTEMI	29	14.5%	
	STEMI	144	72.0%	
CA	**Normal**	12	6.0%	
	PPCI	176	88.0%	
	CABG	12	6.0%	

Table 2: Lab investigations between the three studied groups.

		Diagnosis			Test of significance	
		Unstable angina (N= 27)	**NSTEMI (N= 29)**	**STEMI (N= 144)**		
		Median (IQR) N (%)	**Median (IQR) N (%)**	**Median (IQR) N (%)**	**p-Value**	**Sig.**
CK-MB		17 (14 - 27)	106 (32 - 157)	166.5 (92.5-278.5)	<0.001(K1)	S
CK		119 (83 - 348)	668 (243-1052)	1154 (675.5-3388.5)	<0.001(K1)	S
Albumin		3.8 (3.2 - 4.1)	3.9 (3.5 - 4.1)	3.9 (3.55 - 4.3)	0.088(K)	NS
total protien		6.4 (6 - 7)	6.8 (6.3 - 7.1)	6.5 (6.2 - 7)	0.262(K)	NS
total bilirubin		0.5 (0.4 - 0.8)	0.7 (0.6 - 0.9)	0.7 (0.5 - 0.95)	0.192(K)	NS
Direct bilirubin		0.1 (0.1 - 0.2)	0.2 (0.2 - 0.3)	0.1 (0.1 - 0.2)	0.002(K2)	S
AST		32 (20 - 43)	110 (34 - 195)	221.5 (104.5-438.5)	<0.001(K1)	S
AST ≥2 ULN	**No**	27 (100%) a	12 (41.38%) b	23 (15.97%) c	<0.001(C)	S
	Yes	0 (0%) a	17 (58.62%) b	121 (84.03%) c		
ALT		19 (15 - 30)	33 (22 - 50)	53.5 (27 - 90)	<0.001(K1)	S
ALT ≥2 ULN	**No**	27 (100%) a	28 (96.55%) a	112 (77.78%) b	0.001(F)	S
	Yes	0 (0%) a	1 (3.45%) a	32 (22.22%) b		
Alkaline phosphatase		80 (56 - 89)	85 (67 - 102)	78 (60 - 92)	0.320(K)	NS
Serum creatinine		0.7 (0.5 - 1.1)	0.8 (0.6 - 0.9)	0.7 (0.6 - 0.9)	0.423(K)	NS
Urea		32 (20 - 34)	26 (20 - 34)	28 (22 - 35)	0.559(K)	NS

total cholesterol	125 (103 - 159)	188 (151 - 202)	203.5 (154 - 233.5)	<0.001[K3]	S
LDL	78 (75 - 92.4)	120 (88 - 164)	162 (93 - 172)	<0.001[K3]	S
HDL	56 (42 - 60)	43 (35 - 55)	35 (30 - 50)	<0.001[K3]	S
Triglycerides	92 (80 - 102)	101 (98 - 150)	105 (77 - 160)	0.471[K]	NS
TSH	2.56 (1.54 - 4.21)	2.46 (1.59-3.87)	2.69 (2.13 - 3.54)	0.666[K]	NS
free T3	3.12 (2.55 - 3.45)	2.87 (2.35 - 3.45)	3.12 (2.63 - 3.45)	0.421[K]	NS
free T4	1.27 (1.12 - 1.38)	0.97 (0.68 - 1.32)	1.22 (0.81 - 1.32)	0.020[K3]	S
INR	1.2 (1.08 - 1.3)	1.1 (1.08 - 1.2)	1.1 (1 - 1.2)	0.096[K]	NS

[K] Kruskal Wallis test of significance. *Post-hoc test was significant between: [K1] All groups. [K2] NSTEMI Vs. others. [K3] Unstable angina Vs. others. [C] Chi-Square test of significance. [F] Fisher's Exact test of significance. * Each subscript letter denotes a subset of Group categories whose column proportions do not differ significantly from each other at the .05 level.

Table 3: ECHO findings, in hospital mortality and major adverse cardiac events between the three studied groups.

		Diagnosis			Test of significance	
		Unstable angina (N= 27)	**NSTEMI (N= 29)**	**STEMI (N= 144)**		
		Median (IQR) N (%)	**Median (IQR) N (%)**	**Median (IQR) N (%)**	**p-Value**	**Sig.**
EF%		62% (55% - 64%)	48% (45% - 51%)	40.5% (36% - 48%)	<0.001[K1]	S
LV diastolic function	**Normal**	27 (100%) [a]	19 (65.52%) [b]	35 (24.31%) [c]	<0.001[F]	S
	GI DD	0 (0%) [a]	10 (34.48%) [b]	71 (49.31%) [b]		
	GII DD	0 (0%) [a]	0 (0%) [a]	33 (22.92%) [b]		
	GIII DD	0 (0%) [a]	0 (0%) [a]	5 (3.47%) [a]		
In hospital mortality	**No**	27 (100%)	27 (93.1%)	133 (92.36%)	0.418[C]	NS
	Yes	0 (0%)	2 (6.9%)	11 (7.64%)		
MACES	**Embolic complication**	0 (0%)	0 (0%)	3 (2.08%)	1.00[F]	NS
	Impaired systolic function	0 (0%) [a]	15 (51.72%) [b]	124 (86.11%) [c]	<0.001[C]	S
	RV failure	0 (0%)	0 (0%)	8 (5.56%)	0.281[C]	NS
	Arrhythmias	0 (0%) [a]	1 (3.45%) [a]	45 (31.25%) [b]	<0.001[C]	S

[K] Kruskal Wallis test of significance. *Post-hoc test was significant between: [K1] All groups. [F] Fisher's Exact test of significance. [C] Chi-Square test of significance. * *Each subscript letter denotes a subset of Group categories whose column proportions do not differ significantly from each other at the .05 level.*

Table 4: Demographic data and risk factors between In-hospital mortality groups.

		In hospital mortality		Test of significance	
		Survivors (N= 187)	**Non-survivors (N= 13)**		
		Median (IQR) N (%)	**Median (IQR) N (%)**	**p-Value**	**Sig.**
Age		57 (52 - 64)	64 (57 - 70)	0.014[M]	S
Sex	**Male**	160 (85.56%)	12 (92.31%)	0.699[F]	NS
	Female	27 (14.44%)	1 (7.69%)		
BMI		32 (31 - 35)	32 (31 - 34)	0.916[C]	NS

Smoking	**No**	33 (17.65%)	2 (15.38%)	1.00(F)	NS
	Yes	154 (82.35%)	11 (84.62%)		
DM	**No**	66 (35.29%)	4 (30.77%)	1.00(F)	NS
	Yes	121 (64.71%)	9 (69.23%)		
HTN	**No**	66 (35.29%)	3 (23.08%)	0.549(F)	NS
	Yes	121 (64.71%)	10 (76.92%)		
CA	**Normal**	11 (5.9%)	1 (7.7%)	0.479(F)	NS
	PPCI	165 (88.2%)	11 (84.6%)		
	CABG	11 (5.9%)	1 (7.7%)		

(M) Mann-Whitney test of significance. (F) Fisher's Exact test of significance (C) Chi-Square test of significance.

Table 5: Lab investigations between In-hospital mortality groups

		In hospital mortality		Test of significance	
		Survivors (N= 187)	**Non-survivors (N= 13)**		
		Median (IQR) N (%)	**Median (IQR) N (%)**	**p-Value**	**Sig.**
CK-MB		122 (41 - 236)	266 (118 - 340)	0.036(M)	S
CK		812 (360 - 1978)	4310 (795 - 6548)	0.007(M)	S
Albumin		3.9 (3.5 - 4.2)	3.7 (3.3 - 4.4)	0.905(M)	NS
total protein		6.5 (6.2 - 7)	6.5 (5.8 - 7.6)	0.939(M)	NS
total bilirubin		0.7 (0.5 - 0.9)	0.9 (0.8 - 1.4)	0.008(M)	S
Direct bilirubin		0.1 (0.1 - 0.2)	0.2 (0.1 - 0.3)	0.090(M)	NS
AST		133 (46 - 316)	732 (261 - 1155)	<0.001(M)	S
AST ≥2 ULN	**No**	62 (33.16%)	0 (0%)	0.011(F)	S
	Yes	125 (66.84%)	13 (100%)		
ALT		36 (23 - 69)	176 (156 - 276)	<0.001(M)	S
ALT ≥2 ULN	**No**	166 (88.77%)	1 (7.69%)	<0.001(F)	S
	Yes	21 (11.23%)	12 (92.31%)		
Alkaline phosphatase		79 (64 - 94)	63 (59 - 95)	0.529(M)	NS
Serum creatinine		0.7 (0.6 - 0.9)	0.8 (0.8 - 1.3)	0.003(M)	S
Urea		26 (22 - 34)	35 (34 - 94)	<0.001(M)	S
total cholesterol		189 (142 - 222)	262 (198 - 280)	0.006(M)	S
LDL		131 (84 - 168)	180 (165 - 186)	0.007(M)	S
HDL		42 (31 - 55)	30 (28 - 35)	0.021(M)	S
Triglycerides		100 (80 - 155)	107 (78 - 170)	0.418(M)	NS
TSH		2.69 (1.78 - 3.56)	2.19 (1.98 - 2.59)	0.054(M)	NS
free T3		2.99 (2.55 - 3.45)	2.87 (2.64 - 3.31)	0.927(M)	NS
free T4		1.22 (0.81 - 1.32)	1.26 (0.93 - 1.37)	0.469(M)	NS
INR		1.1 (1 - 1.2)	1.1 (1.1 - 1.2)	0.344(M)	NS

(M) Mann-Whitney test of significance. (F) Fisher's Exact test of significance.

Table 6: ECHO findings and major adverse cardiac events between In-hospital mortality groups.

		In hospital mortality		**Test of significance**	
		Survivors (N= 187)	**Non-survivors (N= 13)**		
		Median (IQR) N (%)	**Median (IQR) N (%)**	**p-Value**	**Sig.**
EF%		45% (39% - 50%)	24% (21% - 28%)	<0.001(M)	S
LV diastolic function	**Normal**	81 (43.32%)	0 (0%)	<0.001(F)	S
	GI DD	79 (42.25%)	2 (15.38%)		
	GII DD	27 (14.44%)	6 (46.15%)		
	GIII DD	0 (0%)	5 (38.46%)		

Embolic complication	**No**	187 (100%)	10 (76.92%)	<0.001(F)	S
	Yes	0 (0%)	3 (23.08%)		
Impaired systolic function	**No**	61 (32.62%)	0 (0%)	0.011(F)	S
	Yes	126 (67.38%)	13 (100%)		
RV failure	**No**	185 (98.93%)	7 (53.85%)	<0.001(F)	S
	Yes	2 (1.07%)	6 (46.15%)		
Arrhythmias	**No**	152 (81.28%)	2 (15.38%)	<0.001(F)	S
	Yes	35 (18.72%)	11 (84.62%)		

(M) Mann-Whitney test of significance (F) Fisher's Exact test of significance.

DISCUSSION

The term "acute coronary syndrome" (ACS) describes an acute ischemia crisis of the heart brought on by a fresh thrombus as a result of the erosion or rupture of an unstable atherosclerotic plaque in the coronary arteries. Acute myocardial infarction (AMI) is also known as ST-segment elevation myocardial infarction, and STEMI or non-STEMI (NSTEMI) **(4)**.

Transaminase elevation is a common occurrence in the current diagnostic and therapeutic age of ACS, it was verified. Additionally, the association between transaminase concentration and enzymatic estimates of infarct size, as determined by troponin I level, was verified **(1)**.

In the current study, the mean age group was 57.79 ± 10.24, with Males represented by 86.0%.

This is in accordance with **Djakpo et al (5)** who investigated the AST/ALT ratio alterations in Chinese Han individuals with acute myocardial infarction who had no history of liver illness. They reported that 28 (23.3%) were female and 92 (76.7%) were male. The mean age was 61.43 (61.43 ±13.702).

In our study, as regards smoking, the results show that the percentage of patients who smoke is highest in the STEMI group (84.72%), followed by the NSTEMI group (82.76%), and the unstable angina group (70.37%) with no statistically significant difference. As regard DM, the results shows that In the STEMI group, the proportion of patients with DM is greatest (73.61%), followed by the NSTEMI group (51.72%), and the unstable angina group (33.33%) with a statistically significant difference.

Li et al (4) reported that 270 STEMI patients (57.0%) had a smoking history, 247 (52.1%) had hypertension, 135 (28.5%) had DM, 47 (9.9%) and among 138 NSTEMI patients (58.0%) had a smoking history, 144 (60.5%) had hypertension, and 81 (34.0%) had DM.

According to our research, there was a substantial difference in the liver enzymes (AST and ALT) between all groups. The percentage of patients who had AST ≥2 ULN and ALT ≥2 ULN was a significant increase in the STEMI group.

This agrees with **Jasiewicz et al (1)** who aimed to assess the blood transaminase levels in ACS and compare them to the generally accepted AST/ALT exclusion standards from clinical trials. They found that the majority of patients with serious myocardial damage have transaminase levels that are more than 3 times ULN. The De-Ritis ratio was high in the current investigation at every time point because AST concentrations were generally greater than ALT concentrations.

It is now clear that cardiac rather than hepatic origin is predominantly responsible for AST and ALT release in ACS patients. **Lofthus et al(2)** validated the baseline increase of AST in 85.6% and ALT in 48.2% of individuals in their extensive research of 1783 patients.

Our results indicate that there was no statistically significant difference in alkaline phosphatase levels between the three groups, (p=0.320).

According to **Oh et al (6),** study aimed to evaluate increased serum transaminases and ALP's combined prognostic significance on admission in STEMI patients who underwent initial percutaneous coronary intervention (PCI). They stated that the majority of patients (almost 95%) had serum ALP levels below the STEMI upper limit of normal.

In this study, in the STEMI group, there was a significant increase in the percentage of patients who had impaired systolic function and arrhythmias while there was no differences in embolic complication and RV failure between the three groups.

It is generally known that NSTEMI is typically associated with around 95% of coronary occlusion while STEMI is frequently associated

with total coronary blockage. **Karwowski et al (7**) a large multicenter observational analysis involving 4581 STEMI and 2717 NSTEMI patients provided late evidence to support this concept. **Djakpo et al(5)** showed that STEMI patients had a higher AST to ALT ratio. In this regard, we anticipated that total occlusion might also be linked to a higher De Ritis ratio.

The present study showed that there was an age rise that was statistically significant within the non-survivor group as the p-Value was <0.05 which is in line with recent data showing that older patients with AMI had a greater mortality rate **(8, 9).**

This also agreed with **Li et al(4**) who found that in AMI patients, the The mortality rate was highly correlated with the patient's age Our study showed that there was a significant increase in Liver enzymes (AST and ALT) in non-survivors and other survivor groups. The percentage of patients who had AST ≥2 ULN and ALT ≥2 ULN was a significant increase in the non-survivor group.

Similar to this, current research indicates that higher serum transaminases are linked to both lower short- and long-term clinical outcomes and more severe myocardial injury (**3).**

According to a few recent investigations, patients with AMI who had increased serum transaminases had worse clinical outcomes. The severity of liver damage, particularly in individuals who already have metabolic syndrome, may directly affect the results of heart surgery **(10).**

In this study, we found that there was a significant increase in cardiac enzymes (CK-MB and CK), in the non-survivors and other survivor group.

This agrees with **Oh et al (6)** who reported that Ineffective results are predicted by peak CK-MB failure.

In our study, regarding the relation between the two hospital mortality groups and ECHO findings, Patients in the non-survivor group had considerably higher degrees of advanced LV diastolic dysfunction than those in the survivor group, and there was a significant decline in EF% in the non-survivor group compared to the survivor group. Additionally, among the non-survivors, it had a significant increase in the percentage of patients who had complications (embolic complications, impaired systolic function, RV failure, and arrhythmias).

This agrees with **O'Neal et al (11)** who investigated the association between echocardiographic parameters, including EF%, and early in-hospital heart failure in people who have had their first STEMI. The findings demonstrated that an elevated risk of early in-hospital cardiac failure was strongly related with a lower EF%.

Similarly, another study investigated the association between LV diastolic dysfunction Regarding the results of acute myocardial infarction patients when they were hospitalized. The results showed that patients with LV diastolic dysfunction had a significantly greater potential for hospital mortality and that the risk increased with the severity of diastolic dysfunction **(12).**

In harmony, **Goyal et al (12**) investigated the clinical characteristics Considering the outcomes of individuals with acute coronary syndromes and impairment of the left ventricle while they were hospitalized. The findings demonstrated a considerably increased risk of in-hospital death in patients with left ventricular systolic failure and that the risk increased with the severity of dysfunction.

Conclusions: ACS patients had significantly increased hepatic transaminases levels. Moreover, Hepatic transaminase levels were strongly correlated with an increased risk of in-hospital all-cause mortality.

Recommendations: Therefore, based on our findings, an effective predictor of an elevated risk of early mortality in ACS patients would be an elevation of the hepatic transaminases, which probably represents HLI. Larger studies with larger scales will be needed to confirm our results.

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