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Left Atrial Remodeling and short-Term Outcome in Patients Presenting with Non- ST Segment Elevation Myocardial Infarction

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ABSTRACT

Background: Non–ST elevation myocardial infarction (NSTEMI) is an acute ischemic event causing cardiomyocyte death by necrosis in a clinical setting consistent with acute myocardial ischemia.

Objective: The aim of the current study was to clarify relationship between left atrial remodeling especially LAVI and short term clinical outcome in patients with acute NSTEMI.

Patients and methods: We conducted this study on 110 non-STEMI patients who were referred to Cardiology Department, Faculty of Medicine, Zagazig University. Echo was performed within 48 hours of non-STEMI and 3 months later. Data were collected and analyzed and patients were divided into 2 groups according to left atrial volume index (LAVI) after 3 months of non-STEMI using cut-off point 34 mL/m^2.

Results: Ejection fraction after 3 months was lower among malone ante grade continence enema (MACE) group with statistically significant difference (p=0.023). Left atrial volume and left atrial volume index were higher among MACE group with statistically significant differences (p=0.0001; 0.0001). Percent of patients with LAVI>34 was higher among MACE group with statistically significant difference (p= 0.0008).

Conclusion: left atrial volume index is a good predictor for incidence of major adverse cardiac events after non-STEMI especially heart failure and angina. At cutoff value equal to 34.2, LAVI exhibited 95.2% sensitivity and 83.2% specificity in predicting incidence of MACE. Determinants of LAVI was baseline left atrial volume, E/A ratio, lesions in left anterior descending and left circumflex artery and ejection fraction after 3 months of non STEMI.

Keywords: Left Atrial, Non–ST elevation myocardial infarction, Heart Disease.

INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD), a chronic inflammatory disorder, is often asymptomatic and has a slow progression during the lifetime of an individual. It can manifest as coronary heart disease (CHD), stroke, peripheral artery disease, and aortic aneurysm. The CHD is the most common form of heart disease encountered in the adults, accounting for 50% of the ASCVD[(1,2)].

Non–ST elevation myocardial infarction (NSTEMI) with resultant sub-endocardial myocardial necrosis represents a group of patients with coronary artery disease (CAD) with a high incidence of future adverse cardiac events. Previous studies have demonstrated that following NSTEMI, there can be associated left atrial (LA) dilatation and abnormal atrial depolarization. However, few studies have systematically examined temporal changes in LA volume or alterations in LA phasic function following NSTEMI. LA remodeling following NSTEMI could increase the occurrence of atrial fibrillation. In the setting of NSTEMI with consequent LV dysfunction, atrial fibrillation could further reduce LV filling, precipitating diastolic heart failure. Therefore, serially monitoring LA volumes and function following NSTEMI may provide valuable prognostic information and enable appropriate targeted treatment. LA function includes phases of reservoir (during ventricular systole), conduit (during early diastole and diastasis), and active contraction (during late diastole) [(3)].

The left atrium modulates left ventricular (LV) filling and cardiovascular performance, acting as a reservoir, a conduit and a contractile pump during the cardiac cycle. Left atrial (LA) size is a marker of LV filling pressure and reflects the severity and chronicity of diastolic dysfunction in those without atrial fibrillation (AF) and significant valvular disease**.** Unlike other Doppler variables of LV diastolic function affected by acute hemodynamic changes, it is a stable parameter that combines the effects of chronic cardiovascular conditions and acute disease[(4)]**.** The Left Atrial Volume Index (LAVI) is a measurement that has gained importance in daily clinical practice due to evidence of its capacity to predict mortality, in patients followed after an Acute Myocardial Infarction (AMI), as well as in the general population[(5)]**.** The left ventricular (LV) function is an important prognostic marker for patients with ACS. The left atrial volume (LAV) is a robust predictor of the CV outcomes and has upcoming evidence supporting its role[(1)]**.**

The aim of this study was to clarify relationship between left atrial remodeling and short term clinical outcome in patients with acute NSTEMI.

PATIENTS AND METHODS

This prospective cohort study was conducted in Cardiology Department, Faculty of Medicine, Zagazig University, on 110 patients diagnosed with acute NSTEMI during the period from March 2022 to August 2022 to determine the relationship of left atrial remodeling with short term clinical outcome and major adverse events following acute NSTEMI.

Ethical consent:

Written informed consents were obtained from all patients and the study was approved by the Research Ethical Committee of Faculty of Medicine, Zagazig University (Institutional review board) ZU-

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IRB # 9323-9-2-2022. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Patients with a diagnosis of acute NSTEMI (defined as presentation with chest pain and an increase in cardiac troponin T, with or without associated electrocardiographic changes **Alpert *et al.*[(6)]** at admission. Patients with age >18 years. Both males and females.

Exclusion criteria included: Patients with STEMI or unstable angina. Patients with a previous history of percutaneous transluminal coronary angioplasty or coronary bypass grafting. Patients with a diagnosis of significant valvular heart disease (more than mild). Patients with advanced kidney and liver disease. patients with a previous diagnosis of cardiomyopathy and heart failure. Patients with chronic or paroxysmal atrial fibrillation, cor pulmonale, malignancy, and anemia. All patients were divided into two groups based on the LAVI value at three months (LAVI=lav/body surface area); Group A: included 18 acute NSTEMI patients (LAVI>34ml/ m^2). Group B: included 92 acute NSTEMI patients (LAVI<34ml/ m^2).

All patients were subjected to full history taking including (name, age, sex, height, weight, body mass index and risk factors of IHD). The baseline and serial electrocardiogram (ECG) was recorded for each patient. Each patient was assessed clinically, echocardiographically at baseline and 3 months and recorded according to New York Heart Association[(Ref)] function class (NYHA). The echocardiography parameters were compared with the initial values and correlated with the newly diagnosed comorbidities and clinical features.

Assessment by echocardiography:

The two-dimensional echocardiography was done within 48h of index NSTEMI admission and at 3 months by vivid 7 machine, probe S3. The LV systolic function was assessed by modified Simpson's disc volumetric method. The biplane method of disks (modified Simpson's rule) is the currently recommended two-dimensional method to assess LVEF[(7)]**.** The diastolic function parameters were assessed simultaneously and correlated with the LAVI. The mitral inflow was assessed with pulsed-wave Doppler echocardiography from the apical 4–chamber view. From the mitral inflow profile, the E- and A-wave velocity, E–deceleration time, and E/A velocity ratio were measured. The tissue Doppler imaging (TDI) of the mitral annulus was also obtained, and e' and a' velocities were measured. The LA function was assessed by the biplane area-length method from apical 4-chamber and 2-chamber views and was indexed for body surface area (figure 1) **[(8)].**

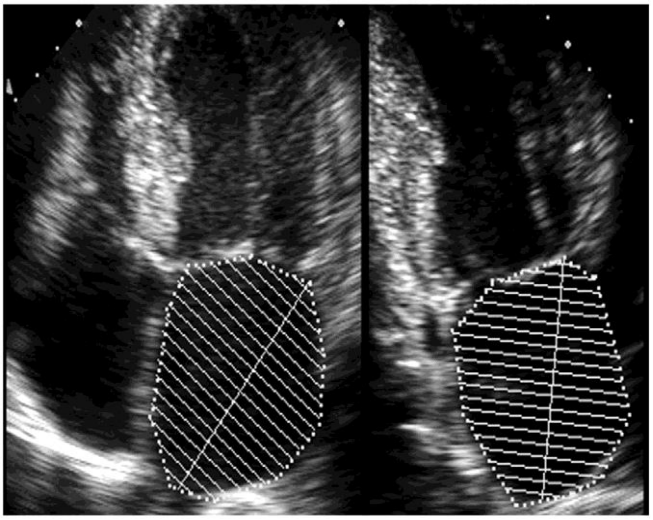

Figure (1): Measurement of LA volume using the biplane method of disks in apical 4- and 2-chamber views.

Coronary angiography: All patients underwent coronary angiography either by radial or femoral route as per the discretion of the treating cardiologist and complete revascularization including culprit and other significant epicardial coronary stenosis.

Follow up: At 3 months Assessment of LV function, diastolic function, LAVI were done for all patients and patients outcome were recorded including death, re-infraction, post MI angina and heart failure.

Statistical analysis

The statistical analysis was done with SPSS statistics. Continuous variables were expressed as mean ± SD standard deviation unless otherwise specified and the categorical variables as percentages. The Student's t-test was used for comparison of two means and Chi square test was used for the categorical variables. A P <0.05 was considered statistically significant. The correlation coefficient (Karl Pearson r) was done for the correlation of the LAVI with the comorbidities and the diastolic function parameters. The receiver operating characteristic (ROC) curve analysis was done for assessing the specificity and sensitivity of the LAVI in ACS patients. Univariate and multivariate regression analysis was done for assessing the independent predictors of coronary artery disease (CAD).

RESULTS

There was statistically significant difference between both groups regarding sex as patients with LAVI>34 had female percent higher than the other group and patients with LAVI<34 had male predominance *(p=0.016).* There were no statistically significant differences between both groups regarding age. There was statistically significant difference between both groups regarding incidence of diabetes (p= 0.01). There was also statistically significant difference between both groups regarding smoking (p=0.005) and dyslipidemia (p=0.048) while no statistically significant difference was found regarding hypertension and presence of positive family history **(table 1)**.

Table (1): Demographics and baseline characteristics:

	Group A (LAVI>34) (no= 18)	Group B (LAVI<34) (n= 92)	Test of Significance	P value
Sex: no. (%) Male Female	 10 (55.56%) 8 (44.44%)	 75 (81.5%) 17 (18.5%)	X^2= 5.79	*0.016*
Age (years) mean±SD	69.33±11.2	60.4±12.5	T= 1.85	0.07
Diabetes no. (%)	15 (83.33%)	47 (51.5%)	X^2= 6.4	*0.01*
Hypertension no. (%)	10 (55.56%)	53 (57.6%)	X^2= 0.025	0.87
Smoking no. (%)	5 (27.77%)	58 (63.04%)	X^2=7.6	*0.005*
Dyslipidemia no. (%)	0	25 (27.17%)	X^2= 3.8	0.048
Family history no. (%)	3 (16.67%)	33 (35.9%)	X^2= 2.5	0.11

LAVI: Left atrial volume index; X^2 Chi- square; t student t-test; Level of significance< 0.05

There were no statistically significant differences between both groups regarding ECG findings, ECHO findings (EF, left atrial diameter, left atrial volume, left atrial volume index), E/A ratio, E/E ratio, deceleration time and grades of diastolic dysfunction **(table 2)**.

Table (2): Cardiac evaluation at baseline:

	Group A (LAVI>34) (no= 18)	Group B (LAVI<34) (n= 92)	Test of Significance	P value
ECG no. (%): Anterior septal Lateral Inferior Anterior & Lateral Lateral & Inferior Diffuse	 0 5 (27.7%) 3 (16.67%) 2 (11.1%) 8 (7.7%) 0	 14 (15.2%) 14 (15.2%) 3 (3%) 25 (27.2%) 26 (28.2%) 10 (10.8%)	X^2= 8.7	0.067
NYHA classification no. (%) 1 2 3	 5 (27.7%) 9 (50%) 4 (22.3)	 24 (26.2%) 40 (43.4%) 28 (30.4%)	X^2= 0.5	0.77
ECHO mean±SD: EF (%) LAD (cm) LAV (mL) LAVI (mL/m^2)	 64.14±5.14 3.16±0.34 54.84±11.6 28.8±1.34	 62.9±12.5 3.14±0.87 41.21±9.8 21.68±2.6	 T= 0.24 T= 0.052 T= 3.23 T= 11.29	 0.68 0.93 0.02 *0.0001*
E/A ratio mean±SD	0.77±0.13	0.84±0.13	T= -1.3	0.2
E/E ratio	16±3.4	16±3.3	T= 0.99	0.5
Decelaration time (msec)	193±44	192±41	T= 0.09	0.92
Diastolic dysfunction grade no. (%): 0 1 2 3	 2 (11.1%) 7 (38.9%) 7 (38.9%) 2 (11.1%)	 19 (20.65%) 28 (30.4%) 41 (44.6%) 4 (4.4%)	X^2= 2.4	0.4

EF: Ejection fraction; LAD: Left atrial diameter; LAV: Left atrial volume; LAVI: Left atrial volume index; X^2 Chi-square; t student t-test; Level of significance< 0.05

There was no statistically significant difference between both groups regarding the culprit lesions and non-culprit lesions **(Table 3)**.

Table (3): Intervention:

	Group A (LAVI>34) (no= 18) No. (%)	Group B (LAVI<34) (n= 92) N0. (%)	Test of Significance (X^2)	P value
Number of culprit lesions	18 (100%)	92 (100%)		
Type of culprit lesions: LAD RCA LCX LAD+RCA RCA+LCX LAD+LCX 3-vessel	 5 (27.78%) 0 8 (44.44%) 0 3 (16.67%) 2 (11.11%) 0	 31 (33.7%) 8 (8.7%) 20 (21.7%) 14 (15.2%) 8 (8.7%) 5 (5.4%) 6 (6.5%)	4.8	0.09
Number of non- culprit lesions	3 (16.67%)	22 (23.9%)	1.9	0.7
Type of non- culprit lesions: LAD RCA LCX RCA+LCX	 0 2 (11.11%) 1 (5.55%) 0	 11 (11.9%) 6 (6.6%) 3 (3.3%) 2 (2.2%)	1.59	0.66

LAD: Left anterior descending; RCA: Right coronary artery; LCX: Left circumflex artery; X^2 Chi-square test; Level of significance< 0.05

There were no statistically significant differences between both groups regarding ejection fraction 3 months after intervention. Left atrial diameter was higher with statistically significant difference among LAVI>34 than LAVI<34 groups (p= 0.001). Left atrial volume and left atrial volume index were higher among group A with statistically significant differences (p= 0.003; 0.0001 resp.).There were no statistically significant differences between both groups regarding E/A ratio, E/E ratio and deceleration time. There was no statistically significant difference between both groups regarding diastolic dysfunction grades 3 months after intervention **(Table 4)**.

Table (4): Echo findings 3 months later:

	Group A (LAVI>34) (no= 18) mean±SD	**Group B (LAVI<34) (n= 92) mean±SD**	**Test of Significance**	**P value$**
EF (%)	57±13.3	64.75±5.7	T= -2.5	0.17
LAD (cm)	3.6±0.37	3.3±0.34	T= -3.375	**0.001**
LAV (mL)	82.68±18.36	44.24±14.68	T= 5.7	**0.003**
LAVI (mL/m^2)	35.22±0.67	23.28±4.9	T= 11.08	**0.0001**
E/A ratio mean±SD	0.95±0.13	1.0±0.13	T= -1.4	0.13
E/E ratio	16±3.21	16±3.31	T= 0.99	0.5
Decelaration time (msec)	202±44	205±41	T= 0.27	0.87
Diastolic dysfunction grades: 0 1 2 3	 1(5.5%) 3 (16.6%) 11 (61.2%) 3 (61.6%)	 14 (15.2%) 23 (25%) 48 (52.2%) 7 (7.6%)	X^2= 2.4	0.3

EF: Ejection fraction; LAD: Left atrial diameter; LAV: Left atrial volume; LAVI: Left atrial volume index; t student t-test; X^2 Chi square test; Level of significance< 0.05

Major adverse events (MACE) were reported in 14 cases in total cohort. MACE was higher among group A with statistically significant difference (p=0.0001). Heart failure incidence was higher among group A with statistically significant difference (p=0.001). Angina incidence was higher among group A with statistically significant difference (p=0.03). No cases of re- infarction or death were reported **(table 5)**.

Table (5): Outcome and incidence of MACE:

	Group A (LAVI>34) (no= 18) No. (%)	Group B (LAVI<34) (n= 33) No. (%)	Test of Significance	P value
MACE	11 (61.11%)	3 (3.3%)	X^2= 45.34	0.0001
Heart failure	8 (44.4%)	3 (3.3%)	X^2= 28.37	0.001
Re-infarction	0	0		
Angina	3 (16.67%)	0	F= 4.8	0.03
Death	0	0		

MACE: Major adverse events; X^2 Chi-square test; F Fisher exact; Level of significance <0.05

Ejection fraction after 3 months was lower among MACE group with statistically significant difference (p= 0.023). Left atrial volume and left atrial volume index were higher among MACE group with statistically significant differences (p=0.0001; 0.0001). Percent of patients with LAVI>34 was higher among MACE group with statistically significant difference (p= 0.0008)). E/A ratio was higher significantly among MACE group than no MACE group (p= 0.003) while both groups were comparable regarding E/E ratio and deceleration time. There was no statistically significant difference between both groups regarding distribution of different grades of diastolic dysfunction **(table 6)**.

Table (6): Echo findings 3 months later:

	MACE (no= 14)	No MACE (n= 96)	Test of Significance	P value
EF (%)	48.4±10.76	65.54±4.55	T= -6.5	***0.023***
LAD (cm)	3.46±0.28	3.25±0.35	T= 1.26	0.187
LAV (mL)	96.57±9.25	44.46±9.6	T= 8.3	***0.0001***
LAVI (mL/m^2)	34.5±2.1	24.36±2.07	T= 5.8	***0.0001***
LAVI >34 No. (%)	11 (78.6%)	7 (7.3%)	X^2= 15.46	***0.0008***
E/A ratio mean±SD	0.9±0.13	1.0±0.13	T= 3.2	***0.003***
E/E ratio	16±3.2	16±3.11	T= 0.99	0.5
Decelaration time (msec)	202±44	205±41	T= 0.27	0.87
Diastolic dysfunction grade no. (%):				
0	1 (7.14%)	14 (14.6%)		
1	3 (21.4%)	23 (41.07%)	X^2= 4.75	0.19
2	8 (23.5%)	51 (53.13%)		
3	2 (14.3%)	8 (8.33%)		

EF: Ejection fraction; LAD: Left atrial diameter; LAV: Left atrial volume; LAVI: Left atrial volume index; X^2 Chi- square; t student t-test; Fx: Fisher exact test; Level of significance< 0.05

DISCUSSION

After dividing patients into 2 groups, group A with LAVI>34 included 18 patients and group B with LAVI<34 included 92 patients. In the current study left atrial remodeling after 3 months of non STEMI reflected by increased LAVI occurred in 16.3% of the non STEMI patients. Like our study, recent study by **Thadani *et al.*[9]** reported 21% of MI patients were followed by atrial remodeling with increased LAVI above 34 ml/m^2. On the other hand, higher percent was reported in another Egyptian study by **Naseem *et al.*[10]** who found that left side remodeling occurred in 31% of the patients. Also, **Moller *et al.*[11]** reported increased LAVI above 32 ml/m^2 in about 45% of the included patients. However, both studies included STEMI and non- STEMI patients.

In the current study, patient age was much higher among elevated LAVI group than the other group but the difference of no statistically significance. However, in total cohort, there was statistically significant positive correlation between LAVI and age. Similarly, **Thadani *et al.*[9]** reported statistically significant positive correlation between age and LAVI after myocardial infarction.

Increased LAVI above 34 was reported more frequently by females (44.44%) than males (18.5%) with statistically significant difference. However, on comparison male and females in total cohort, mean values of LAVI were comparable. Similar to this results, **Pritchett *et al.*[12]**, found statistically significant association between left atrial volume and female gender.

Smoking was more frequent among non-elevated LAVI group with statistically significant difference in our result. **Moller *et al.*[11]**, reported the same findings that suggests that smoking was associated with impaired remodeling after MI.

Regarding associated medical disorders, both groups were comparable regarding incidence of hypertension while diabetes was associated with increased LAVI and dyslipidemia was associated significantly with decreased LAVI in the current study. **Moller *et al.*[11]**, came in hand with us regarding the association between LAVI and diabetes while against our result, he found statistically significant correlation with hypertension and failed to demonstrate any association with dyslipidemia. In contrary to the current study, **Thadani *et al.*[9]** did not report any significant association between LAVI and other comorbidities as hypertension, diabetes and dyslipidemia**.**

Regarding baseline Echo findings, there were no statistically significant differences between both groups regarding ejection fraction and left atrial diameter while left atrial volume was the main predictor for increased LAVI with statistically significant difference between both groups. In concordance to the current study, **Thadani *et al.*[9]** reported that left atrial volume was the main indicator for the LAVI among left atrial Echo findings. He reported also that left ventricular volume, mass and mass index increased with increased LAVI. **Moller *et al.*[11]**, showed that both left atrial diameter and volume increased significantly with elevated LAVI**.**

There was no statistically significant difference between both groups regarding diastolic dysfunction grades at baseline. On the other hand, **Thadani *et al.*[9]** reported increased cases of diastolic dysfunction among high LAVI group. Also, **Moller *et al.*[11]**, found higher percent of normal diastolic function patients among LAVI <34 while percent of grade 3 diastolic dysfunction patients were higher among LAVI>34 while incidence of grade 1 and 2 were comparable.

In the current study, there was no statistically significant difference between both groups regarding type of involved artery and the highest frequency was the left anterior descending followed by left circumflex coronary arteries. This comes in hand with **Roth and Elkayam[13]**, which stated that the vast majority of MI involves the anterior wall (78%) **Roth and Elkayam[13]** and **Shahzad *et al.*[14]**, who proposed that the most common coronary artery affected is the left anterior descending (LAD) branch. The left anterior descending artery was the most common culprit artery (48.3%), followed by the right coronary artery (30.9%), and the circumflex artery (20.8%) in a study [15].

In the current study, there was no statistically significant difference between different lesions regarding LAVI. **Janwanishstaporn *et al.*[16]**, also did no report significant difference between variable coronary lesions regarding LAVI. Also, **Beinart *et al.*[17]**, reported high incidence of anterior wall ischemia with left anterior descending affection with no difference between low and high LAVI.

After 3 months of non STEMI, there was no statistically significant difference between both groups regarding ejection fraction against what was reported in previous studies who reported that high LAVI was associated with poor prognosis in patients with reduced EF[10,11,16,17]. They explained their results by the associated between left atrial remodeling and left ventricular changes in mass and volume which by turn affected the ejection fraction.

There was no statistically significant difference between both groups regarding prevalence of different grades of diastolic dysfunction.

In contrary to the current study, **Matsuda *et al.*[18]**, demonstrated that LA maximal volume increased with increasing severity of DD as defined by invasive hemodynamic study. Previously, **Nishimura *et al.*[19]**, demonstrated that increasing LA pressure positively correlated with Doppler evidence of DD in a group of patients with cardiomyopathy and EF<40%. **Pritchett *et al.*[12]**, reported also that increased LAVI was associated with increased diastolic dysfunction grade after remodeling.

Regarding outcome, MACE in the form of heart failure and angina had higher frequency among elevated LAVI group than low LAVI group.

The explanation why LAVI could predict incidence of MACE could be referred to multiple causes; First, LA volume reflects the duration and severity of increased LA pressure. Second, apparently normal filling patterns may be associated with significant elevation of LV filling pressures These "pseudonormal" filling patterns have been associated with increased mortality after AMI but may be difficult to identify with standard Doppler techniques. In contrast, LA volume index may better differentiate such patient[11].

In accordance to the current studies, multiple previous researches reported elevated LAVI is a good predictor for incidence of MACE after MI during remodeling[9,11,16, 17]. **Seko *et al.*[20]**, reported that the cumulative 3-year incidences of the primary outcome measures and MACE were significantly higher in the high-LAVI group than for the normal group. The excess risk of heart failure (HF) and unstable angina pectoris in the high-LAVI group relative to that in normal group remained significant among MACEs[20].

Previous studies demonstrated that LA volume >34 ml/m^2 (normal value ± 2SD) was an independent predictor of adverse events after MI [21,22].

The study had the advantage of being performed on relative large sample size and evaluated different demographic, clinical, radiological and laboratory predictors for elevated left atrial volume index and for incidence of MACE.

Study limitations: The study had some limitations as lack of randomization and absence of healthy control group.

CONCLUSION

Left atrial volume index is a good predictor for incidence of major adverse cardiac events after non STEMI especially heart failure and angina. At cutoff value equal to 34.2, LAVI exhibited 95.2% sensitivity and 83.2% specificity in predicting incidence of MACE. Determinants of LAVI was baseline left atrial volume, E/A ratio, lesions in left anterior descending and left circumflex artery and ejection fraction after 3 months of non STEMI.

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Author contribution: Authors contributed equally in the study.

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