A Relationship of Caveolin-1 with Lipid Profile and a Number of Anthropometric Measurements in Iraqi Myocardial Infarction Patients

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Abstract
Myocardial infarction (MI) represents the most common death and morbidity cause all over the world, as it is responsible for as many as 40% of all of the death cases. Atherosclerotic inflammation has a role in the formation of coronary plaque as well as its advancement to unstable state, which results in causing MI. In the present study, there is an attempt for measuring whether there are any associations of the Caveolin-1 (CAV-1) with lipid profile parameters and some anthropometric measurements (AMs) such as waist / hip (W /H), waist/ thoracic (W /T), and waist/ nick (W /N) in Iraqi MI patients. This study involved 42 MI patients from Al-Fallujah teaching hospitals, in addition to 42 healthy people who served as controls. ELISA was used for the purpose of determining the level of CAV-1 in the serum, while TG, T.Cho, HDL, CPK (MB), and cTn-T were determined by enzymatic colorimetric methods. Serum level of CAV-1 has been lower in MI patients when compared with it in the healthy people (P< 0.000l), but cTn-T and CPK (MB) compared to HCs, were considerably greater in MI patients. (P < 0.000l). CAV-1 has an important negative correlation with cTn-T, CPK (MB), LDL/HDL and TC/HDL (P< 0.000l), while it showed positive correlation with HDL (P < 0.000l). The studied parameters showed the descending order of the area under receiver operating characteristic (AUROC) curve: cTn-T was (1), CPK (MB) (1), CAV-1(0.913), HDL (0.999), T. Cho. /HDL (0.905), TG (0.891), VLDL (0.891) LDL (0.721), W/H (0.804), W/N (0.727), W/T (0.661). Serum CAV-1level can be used as a novel biomarker in the detection of MI and may be an effective biomarker in the diagnostic test MI.
Keywords: caveolin-1; myocardial infarction patients; lipid profile

1. Introduction

Myocardial infarction is the most prevalent death cause in the world. It has been characterized by myocardial necrosis as a result of acute myocardial ischemia [1]. Typical ischemia symptoms, elevations in the levels of myocardial necrosis biomarkers and abnormal Q waves on the electrocardiogram (ECG) can all be used to diagnose MI [2]. High blood pressure, smoking, dyslipidemia, diabetes and obesity are major risk factors for MI [3]. At the tissue and organ levels, the pathophysiologic course of MI consists of two linked processes: infarct repair and cardiac remodeling [4].

There are 3 isomers in caveolin family caveolin-1, -2 and -3. Caveolin-1 (CAV1) is an essential membrane protein found in endothelial cells (ECs), adipocytes, pneumocytes, muscle cells and fibroblasts [5]. It is involved in many physiological and pathological processes such inflammation, antifibrosis and oxidative stress [6].MI can worsen heart disease by reducing coronary blood flow and oxygen levels. Moreover, in renal and cerebral ischemia, caveolin expression changes ischemic damage. This damage is prevented by caveolins. Cav-1 deficiency causes contractility loss via disrupting adrenergic signaling [7].

Caveolin-1 is a key pathophysiological component in progression of atherosclerosis (AS). Recent research had demonstrated that CAV-1 have a pathogenic role in AS through regulating membrane trafficking, cholesterol metabolism and cellular signal transduction [8]. CAV-1 deficiency has been linked to enhanced cholesterol ester absorption, acyl-CoA: cholesterol acyl-transferase activities, one of previous study had discovered that CAV-1-deficient (CAV-1) mice displayed improved levels of plasma triglyceride (TG), increase in the levels of the high-density lipoprotein (HDL) and decreased secretion of the hepatic very low-density lipoprotein (VLDL). They also found that CAV-1 deficiency prevented transcytosis of low-density lipoprotein (LDL) across ECs, which suggested the fact that the CAV-1 could be implicated in regulating the levels of plasma LDL and, as a result, could be playing a significant role in developing AS [9].

Caveolin-1 has a significant impact on cancer disease. New study demonstrated that CAV-1 in pancreatic cancer patients stimulated insulin-like growth factor-1receptor (IGF1R) and glycolysis in cancer cells and triggered cachectic states in tumor carrier [10].

The body mass index (BMI) scale is the finest public AMs for measuring obesity (which measures by dividing weight in kg on height by meter squared). World Health Organization (WHO). AMs such as waist/hip ratio (W/H), waist circumference (WC), and high levels of T.Cho., TGs, LDL, VLDL with low levels of HDL were considered independent risk factors for cardiovascular disease (CAD) and MI infection [11, 12].

The major goal of this study has been aimed towards the determination of serum level of CAV-1in MI patients and control to explore the correlation

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between CAV-1 with a number of bio-parameters in Iraqi MI patients.

2. Materials and Methods

This study involves eighty-four subjects, forty-two of them were with MI infection which was diagnosed with ECG and cardiac biomarkers (troponin T) and creatinine phospho kinase (CPK) MB, and forty-two persons were recorded in the study as healthy controls (HCs), matching with patients in age, sex and ethnic background, the age range for all subjects were (35-65) years, chosen from Al-Fallujah teaching hospital between November 2021 to April 2022. To determine the concentrations of CAV-1 in the subjects, we used ELISA kits (BT LAB Inc, China)

All study participants had AMs. BMI has been calculated through the division of the value of the weight (kg) by the squared value of the height (m2). The WC, thoracic circumference (TC), nick circumference (NC) and hip circumference (H C) were measured. Moreover, the waist to hip circumference ratio (WC/HC) was also determined.

3. Statistics

GraphPad Prism version 7.04 was used to conduct statistical analyses of these findings (GraphPad Software, La Jolla, CA, USA). The mean, standard error of mean (SEM) and standard deviation (SD) are stated as the consequences. The t-test has been utilized in order to evaluate whether the differences between the subjects were statistically significant. Bivariate associations were tested using two-tailed Pearson correlations, but precision of research has been determined using area under curve (AUC) of receiver operating characteristic (ROC) curve. P 0.050 has been determined as statistically significant.

4. Results

Table1, states standard practical features of subjects which have been described, with average age of 37.00 years in the healthy controls and 19.30 years in the patients of MI (P =0.0709) (Fig.1). MI patients had significantly higher BMI, W/H, W/T and W/N compared to it in the healthy control geoup with P < 0.000l0 for BMI, W/H while W/T had p=0.0056, and W/N had (p=0.0004) (Figs 2, 3 and 4) respectively. SBP, DBP, and ROP levels of MI patients have been considerably higher compared to the healthy control group with P less than 0.000l0 for all of the parameters (Figs 5, 6 and 7) respectively.

The results demonstrated that MI patients had significant lower serum CAV-1 levels (ng/mL) compared to HCs (p<0.0001) (Fig.8), serum level of troponin-T and CPK-MB (ng/mL) were importantly higher in the patients when compared to HCs (p<0.0001) (Figs 9 and 10) respectively, there were significant difference in total cholesterol (T. Cho.) and TG (mg/dL) with p-value of T. Cho (p= 0.0016) and TG (p<0.0001) (Figs 11 and 12) respectively, however HDL was lower in MI patients than HCs (p<0.0001) (Fig.13). The current study also found that in MI cases, LDL and VLDL levels have been non-significantly higher than in HC in both LDL (P=0.0010) and VLDL (P<0.0001) (Figs 14 and 15) respectively. Mean arterial pressure (MAP) was higher in patients compared HCs (p<0.0001) (Fig.16)., also this study showed the levels of LDL/HDL and T. Cho. /HDL, they have been considerably higher in MI cases greater than in HCs. with p<0.0001 for these two variables (Figs 17 and 18) respectively.

Table1: Distribution of the Studied Bio-markers in the healthy controls and MI Patient Groups.

Parameters	HC group			Patient group			pvalue
	Mean	SD	SEM	Mean	SD	SEM	
Cavolin-1 ng/mL	37.00	14.56	2.246	19.30	5.975	0.9220	<0.0001
Troponin-ng/mL	0.0350	0.0125	0.0019	16.99	5.818	0.8977	<0.0001
CPK-MB ng/mL	0.1929	0.0947	0.0146	50.86	21.30	3.289	<0.0001
T. Cho. mg/dL	154.9	27.22	4.201	177.6	35.70	5.508	0.0016
TG mg/dL	115.1	23.82	3.676	174.4	52.10	8.040	<0.0001
HDL mg/dL	48.84	4.210	0.6497	33.47	5.843	0.9016	<0.0001
LDL mg/dL	83.75	28.03	4.325	109.9	41.00	6.326	0.0010
VLDL mg/dL	23.01	4.765	0.7353	34.87	10.42	1.608	<0.0001
LDL/HDL	1.728	0.0948	0.6145	3.268	1.129	0.1743	<0.0001
T. Cho./HDL	3.204	0.6822	0.1053	5.637	2.423	0.3739	<0.0001
W /H	0 .9445	0 .0657	0 .0104	1 .016	0 .0513	0.0079	<0.00 01
Age years	48.31	7.396	1.141	51.38	7.975	1.231	0.0709
BMI Kg/m2	24.61	1.352	0.2086	27.37	3.275	0.5053	<0.0001
DBP mmHg	80.95	4.542	0.7009	91.60	10.47	1.616	<0.0001
W /T	0 .9896	0 .0521	0 .0080	1 .019	0.0435	0.006	0 .0056
SBP mmHg	124.5	8.802	1.358	144.6	16.76	2.586	<0.0001
W /N	2 .435	0 .1674	0 .0258	2 .558	0.1375	0.0212	0 .0004
MAP mmHg	95.46	4.563	0.7041	109.3	11.54	1.780	<0.0001
ROP 1/Min	75.71	2.932	0.4525	80.62	5.992	0.9245	<0.0001

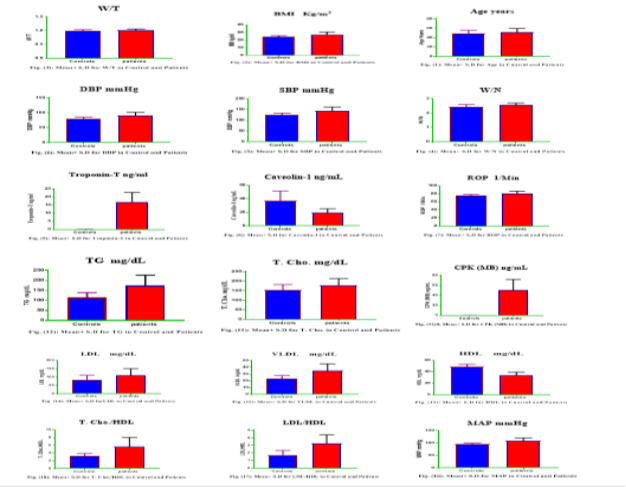
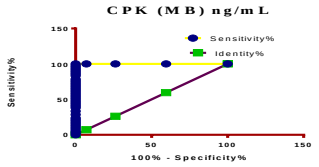


Table 2: Association of CAV-1 with Studied Parameters		
Correlation of Caveolin-1 with all Studied Parameters		
Parameter	r (Caveolin-1 ng/mL)	p-value
Caveolin-1 ng/mL	1.000	0.0000
Troponin-T ng/mL	-0.539	<0.0010
CPK-MB ng/mL	-0.535	<0.0010
SBP mmHg	-0.227	0.0380
DBP mmHg	-0.330	0.0020
ROP 1/Min	-0.192	0.0800
MAP mmHg	-0.304	0.0050
T.C mg/dL	-0.237	0.0300
TG mg/dL	-0.350	0.0010
HDL mg/dL	0.583	<0.0010
LDL mg/dL	-0.297	0.0060
VLDL mg/dL	-0.350	0.0010
LDL/HDL	-0.370	<0.0010
T.Cho./HDL	-0.402	<0.0010
Age years	-0.173	0.1150
W /H	-0 .287	0 .0080
W /T	-0 .144	0 .1900
W /N	-0 .248	0 .0230
BMI kg/m^2	-0.323	0.0030

Important negative correlation was detected between CAV-1 with troponin-T and CPK-MB HDL (r= -0.583, P<0.0010),(r= -0.535, p<0.0010) respectively, also negative correlations of CAV-1 with BIM, W/ H, W/ T and W/ N (r = -0.323, p = 0.003) (r = -0.287, p = 0.008), (r = -0.144, p=0.190), (r= -0 .248, p=0.023) and also negative correlation of CAV-1 with T.C, TG, LDL, VLDL, LDL/HDL and TC/HDL (r=-0.237, p=0.030), (r=-0.350, p=0.0010), (r=-0.297, p=0.006) respectively as well SBP, DBP, ROP, MAP, and Age (r=-0.227, p=0.038), (r=-0.330, p=0.002), (r=-0.192, p=0.080), (r=-0.304, p=0.005), (r=-0.1730, p=0.115) respectively, while positive relationship between HDL with CAV-1(r= 0.583, p<0.0010) was detected as shown in table 2.

Troponin-T and CPK-MB were found to be the best indicators for distinguishing MI patients from HCs using ROC curve analysis [AUS 1; P<0.00010; 95% Confidence Interval (CI): 1 to 1 and SE: 0] as show in as shown in table3 (figures 18 and 19 respectively), also CAV-1 was established to be a better predicator for MI [AUC =0 .913; P = <0.00010; 95% CI: 0.8541 to 0.9718and SE: 0.01554] as displayed in table3 (figure 20), while (SBP, DBP, ROP, MAP, TG, HDL, LDL, VLDL, LDL/HDL and T. Cho./HDL) revealed a high level of discriminatory efficacy between healthy individuals and patients. [AUC=0.859; p <0.00010; 95% CI; 0.776 to 0.9423 and SE; 0.0424] figure. 21, [AUC= 0 .828; P <0.00010; 95% CI; 0.7319-0.9245 and SE; 0.0491] figure.22, [AUC = 0 .872; P<0.0001; 95% CI: 0.786-0.9572 and SE; 0.0437] figure.23, [AUC=0.784; P<0.00010; 95% CI: 0.6814 to 0 .8861and SE; 0.0522] figure.24, [AUC=0.999; P<0.00010; 95% CI: 0.9958-1.002 and SE;0.0016] figure.25, [AUC=0.721; P=0.0005; 95% CI:0.6085 to 0.833 and SE;0.0573] figure.26, [AUC=0.891; P <0.00010; 95% CI: 0.8176 to 0.9648 and SE; 0.0376] figure.27, [AUC=0.880; P<0.00010; 95% CI: 0.8034-0.9573 and SE;0.0393] figure. 28, [AUC= 0 .905; P<0.0001; 95% CI: 0.8367-0.9734 and SE; 0.0349] figure.29, respectively. Anthropometric measures (BMI, W /H, W /N) have shown quite good discriminatory effectiveness between the MI patients and the HCs. [AUC= 0.777; P<0.00010; 95% CI: 0.6732-0.8801and SE; 0.0528] figure.30, [AUC=0.804; P<0.00010; 95% CI: 0.7121 to 0.8962 and SE; 0.0469] figure.31, [AUC=0.727; P=0.0004; 95% CI: 0.6156-0.8356 and SE; 0.0561] figure.32, While T. Cho, W/T and Age showed low validity in predicting validity [AUC=0.696; P=0.0020; 95% CI: 0.5822-0.8101 and SE; 0.0582] figure.33, [AUC= 0.661; 95% CI: 0.0598 to 0.7779 and SE; 0.0112] figure. .34 And [AUC = 0 .625; 95% CI: 0.5052 to 0.7448 and SE; 0.0485] figure 35.

Table3. AUC for all of the Bio-markers that have been analyzed				
Parameters	AUC	Standard Error	95% interval of confidence	Pvalue
Caveolin-1 ng/mL	0.913	0.0300	0.8541-0.9718	<0.00010
Troponin-T ng/mL	1	0	1-1	<0.00010
CPK-MB ng/mL	1	0	1-1	<0.00010
T. Cho. mg /dL	0 .696	0 .0582	0 .5822-0 .8101	0.00200
TG mg /dL	0 .891	0 .0376	0 .8176-0 .9648	<0.00010
HDL mg /dL	0 .999	0 .0016	0 .9958-1.002	<0.00010
LDL mg /dL	0 .721	0 .0573	0 .6085-0 .8332	0.00050
VLDL mg /dL	0 .891	.0376	0 .8176-0 .9648	<0.00010
LDL /HDL	0 .880	0 .0393	0 .8034-0 .9573	<0.00010
T. Cho./HDL	0.905	0.0349	0.8367-0.9734	<0.00010
Age years	0.625	0.0611	0.5052-0.7448	0.04850
BMI Kg/m^2	0.777	0 .0528	0 .6732-0.8801	<0.00010
W/H	0 .804	0 .0469	0 .7121-0.8962	<0.00010
W/T	0 .661	0 .0598	0 .5436-0.7779	0 .01120
W/N	0 .727	0 .0561	0 .6156-0.8356	0 .00040
SBP mmHg	0 .859	0 .0424	0 .776-0.9423	<0.00010
DBP mmHg	0 .828	0 .0491	0 .7319-0.9245	<0.00010
MAP mmHg	0 .872	0 .0437	0 .786-0.9572	<0.00010
ROP 1/Min	0.784	0.0522	0.6814-0.8861	<0.00010



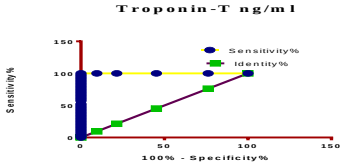
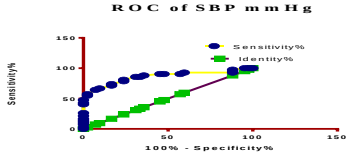


Figure18: Area under the curve of Troponin-T *Figure19: Area under the curve of CPK (MB)*



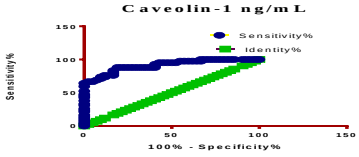
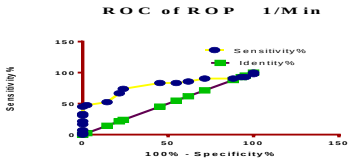


Figure30: Area under the curve of BMI *Figure31: Area under the curve of W /H*



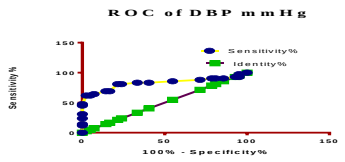
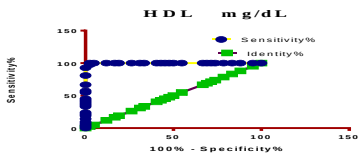


Figure22: Area under the curve of DBP *Figure23: Area under the curve of ROP*



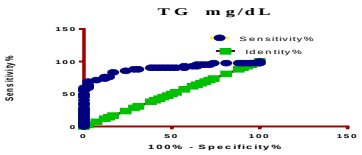
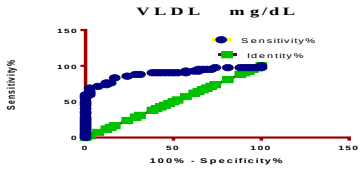


Figure24: Area under the curve of TG *Figure25: Area under the curve of HDL*



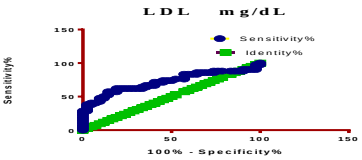
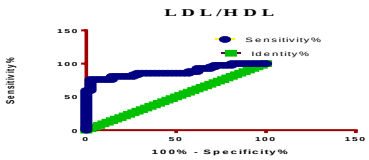


Figure26: Area under the curve of LDL *Figure27: Area under the curve of VLDL*



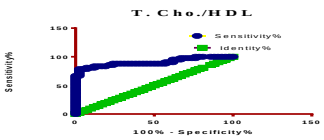
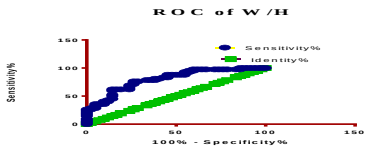


Figure28: Area under the curve of of LDL/HDL *Figure29: Area under the curve of T. Cho. /HDL*



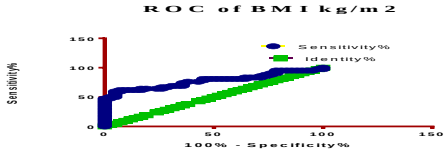
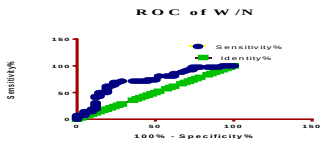


Figure30: Area under the curve of BMI *Figure31: Area under the curve of W /H*



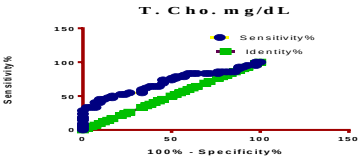
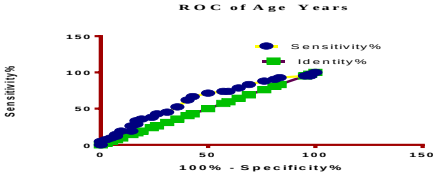


Figure32: Area under the curve of W /N *Figure33: Area under the curve of T. Cho.*



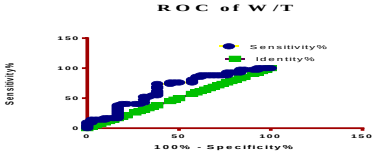


Figure34: Area under the curve of W /T *Figure35: Area under the curve of Age*

5. Discussion

Myocardial Infarction results from the sudden blockage in coronary arteries, which supply heart muscle. The majority of these blockages are caused by atherosclerosis, a condition in which cholesterol and white blood cells build up in the arterial wall [13]. Inflammation and inflammatory cell infiltration are the hallmarks of MI and reperfusion injury. Myocardium inflammation is by a tissular concentration of circulating leucocytes that move through the artery wall into the ischemic myocardial area after being encouraged by the vascular endothelium [14]. Cav-1 and caveolae were discovered to be involved in the immune responses to the inflammation. Cav-1 inhibits the producing and releasing various key inflammatory cytokines, which include the interleukin IL-1, -2, -4, and -12, in addition to the tumor necrosis factor (TNF α) and regulated in the moment of the activation, normal T-cell expressed and secreted (RANTES) [15].

Present study demonstrated a statistically significant decrease in CAV-1 level of MI patients when compared with control. So, CAV-1 deficiency led to decreased contractile dysfunction and cell damage following ischemia in heart that suffer from deficiency in CAV-1 according to Kaakinen M et al [16]. When myocytes die, the sarcolemma membrane becomes permeable to macromolecules like CK-MB and Troponin-T. These macromolecules leak out into the microvasculature and lymphatics at the area of the infraction, eventually being identified in the circulation [17]. Our study presents that severity related biomarkers (Troponin-T and CPK-MB). Troponin is more sensitive and specific for diagnosis in MI. So, it enters the bloodstream 6-8 hrs after a heart attack, reach a plateau between 12 and 24 hours and remain elevated for 7 to 10 days. The enzyme CK-MB is unique to the cardiac tissue. After 4 to 6 hours, myocardial ischemia occurred CK-MB can be detected in serum, albeit it may take up to 12 hours for some persons then it returns to normal within 36 to 48 hours [18].

Dyslipidemia is considered as one of the major risk factors of the CVD. Stress caused by myocardial injury increases adipocytes' adrenergic-mediated lipolysis, resulting in an increase in free fatty acids, TG and lipoproteins. Free fatty acid mobilization and hepatic production of very low-density lipoprotein also raise TG levels [19]. The current results show significant decrease in HDL level of MI patients when compared with control, while T. Cho., TG, LDL and VLDL were increased in MI patients compared with control.

In agreement with a previous study, this study showed that lipid complications contain not only quantitative but also qualitative abnormality of lipoproteins that are likely atherogenic, quantitative abnormalities include elevated levels of overall serum T. Cho, TG, LDL-C, in addition to reduced levels of HDL-C [20].

The anthropometric measure of general obesity, (BMI), is a key risk factor for CVD illnesses. Recent study showed that W/H is the most closely connected with the risk of MI globally among the widely used anthropometric parameters [21]. According to this study, our data also shows the W/H, W/T and W/N are higher in patients with Myocardial infarction compared to the control.

Both diastolic blood pressure (DBP) and systolic blood pressure (SBP) have caused increasing the risk of MI. In this study MAP SBP, ROP and DBP are higher in MI patients than control. So, hypertension hastens the onset of atheroma, increases plaque shear stress, inhibits coronary circulation and compromises endothelial function [22].

6. Conclusion

This study found that serum level of CAV-1 has been noticeably lower in Myocardial infarction patients compared to it in the HCs, and it is strongly related with HDL. Thus, our results revealed that periodic assessment of the serum CAV-1 level could be a good biomarker to predict the risk of MI infection.

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