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The Relationship between Cognitive function and Cardiac Remodeling post-Myocardial Infarction

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Abstract

Myocardial infarction is the main cause of adverse left ventricular (LV) remodellin which was ended by heart failure, There's connection between Cognitive function impairment and heart failure. We assessed the relationship between cognitive function and LV remodelling in ST-segment elevation myocardial infraction (STEMI) patients.

Patient and methodology: A case-control observational study included 33 patients admitted for their first attack of acute STEMI, between November 2020 and May 2021 at Aswan university hospital with different types of management, and a follow-up after two months, the patients were divided according to whether LV remodeling and reduced ejection fraction (EF) were determined on echocardiography. we assessed a cognitive function by using CDT (clock drawing test) with different scoring parameters at acute STEMT stage, and after two months.

Results: The 33 patients (mean aged 53 -/+11 years), 26 males. LV reverse remodelling occurred in 13 (59%) patients, and increase EF in 11 (47.8%) patients, while LV adverse remodeling occurred in 7 (31.8%), and Decrease EF occurred in 4 (17.3%) patients.

By correlation: The cognitive function in the acute stage correlated with the increase EF 2 months post-STEMI. ***(r +0.683, p-value 0.021***), increase cognitive function strongly correlated with increases FE 2 months post-STEMI ***(r + 1, < p-value 0.000).***

By roc curve analysis: Cognitive function could be a predictor of the occurrence of improvement of LV End systolic volume ESV ***AUC 0.685,*** and decrease EF ***AUC 0.737***
2 months post-STEMI.

Conclusion: There is a relationship between cognitive function and LV remodelling in STEMI patients. Cognitive function can be a predictor of reverse LV remodelling and decrease EF two-month post-STEMI.

Keywords Acute myocardial infraction, Remodeling, cognitive function, predictor

Abbreviations

AMI; acute myocardial infarction
CMR; cardiac magnetic resonance,
CDT; a clock drawing test
CKD: chronic renal disease.
2D echocardiography; two-dimensional echocardiography

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EDV; End-diastolic volume,
EF; Ejection fraction,
ESV; End-systolic volume;
ECG; electrocardiogram,
HF; heart failure
LV, left ventricular
LVR, left ventricular remodelling.
MI; myocardial infarction
PPCI; primary percutaneous coronary intervention
STEMI; ST segment elevation myocardial infarction.

Introduction The most common cause of cardiac remodelling is anterior acute myocardial infarction (AMI). Despite the use of primary percutaneous coronary intervention (PPCI) and optimal standard pharmacotherapy, cardiac remodelling ultimately occurs in 30% of anterior AMIs, and in 17% of cases with non-anterior myocardial infarct, cardiac dysfunction is the main consequence of cardiac remodelling [1].

Decline in global cognitive ability tends to be faster after heart failure (HF) diagnosis than without HF. studies have demonstrated that cognitive impairment (CI) is particularly common in HF with 30% to 80% of patients with HF experiencing some degree of cognitive impairment. Most of the patients with HF suffer from mild impairment in cognition whereas about 25% may have moderate-to-severe CI. In addition, HF severity has been linked to increased risk of CI [2-6], while effective treatment of HF, use of angiotensin converting enzyme (ACE) inhibitors, and physical activity lead to improvement in cognitive performance which imply that CI may fluctuate in severity and can also be modified to some degree. [7]. As specialists in meta-analysis suggest that coronary heart disease is associated with increased odds of developing cognitive impairment or dementia, with worldwide increase in the number of people affected by coronary heart diseases and dementia. [8]. We will study the relationship between LV post ST elevation myocardial infarction (STEMI) and cognitive function, we will further try to find a connection between cognitive function and cardiac remodelling, in order to ascertain whether the cognitive function can use as rapid test for prediction of LV remodelling.

AIM OF THE WORK

- To assess the relationship between cognitive function and remodelling in patients after STEMI.

Patients and methods:

Our study included patients with first attack of acute STEMI who were admitted to the cardiology department at Aswan University Hospital between November 2020 and May 2021.

- **Group one** *(patient group)* included 33 patients suffering from their first attack of acute ST-segment elevation myocardial infarction (within 1-7 days of STEMI hospital staying period, with a follow-up 2 months later). All patients with STEMI were treated according to the updated guidelines.

Patients with evidence of prior ischemic heart disease, rheumatic heart disease or valvular heart disease, previous cardiomyopathy (either primary or secondary), congenital heart disease, non-sinus rhythm like AF, patients who had received chemotherapy, patients with a history of neuron or psychiatric problems like

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cognitive disorders or a stroke and patients on medication that affected the acetylcholine level like cholinesterase inhibitors were all excluded from the study.

- **Group two** *(control group)* included 26 healthy subjects. Both groups consisted of patients of the same sex and similar age.

Ethical consideration: A case group and control group participated voluntarily; they gave their informed consent to participate in the study. The study was approved by ethics committee of Aswan university. The declaration of Helsinki was adequately addressed.

- The medical history of patient, and control group in the study were carefully reviewed, and they all underwent a physical examination, routine laboratory investigations, resting ECG and evaluation by 2D echocardiography with an assessed a cognitive function test. The patient group underwent the same tests again 2 months later.

1. 2D Echocardiography studies:

Echocardiography was done while Patient in left lateral decubitus position using transthoracic echocardiography using a standard commercial system (Philips IE 33 Ultrasound) and an X5-1 phased array sector probe. The study was ECG-gated and performed according to the following protocol:

I. A standard echocardiography study (m-mode and biplane Simpson's method) was implemented.

II. Two-dimensional echocardiography was carried out 2 months later for the patients in the study.

The following variables were obtained:

LV end-diastolic volume (EDV), LV end-systolic volume (ESV), LV EF using biplane Simpson's method [9,10].

2. Cognitive function test:

The assessment of Cognitive function was done by using a clock drawing test (CDT) with different score systems for evaluation.

The clock drawing test (CDT) protocol:

- We told 3 words to patient and asked him to recalled them within 3 to 5 minutes, the words were used (photo, garden, kitchen) in arabic languish.
- Provided patient with a piece of paper with a pre-drawn circle of approximately 10 cm in diameter.
- asked the patient to put in the numbers so that it looks like a clock.
- Asked the patient to add arms so that the clock indicates the time "ten minutes after eleven."
- Analysis the results and put Score by using:

1- **Mini-cog test** [11]

The total score = (0-5), Total score = score of words recall + score of clock draw.
Word recall score (0-3) one point for each word spontaneously recalled, then clock draw score (0-2), normal clock = 2 and abnormal = 0.
A total score of more than (3) was considered normal.

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2 **Shulman et al method.** [12]

Is a clock-drawing test (CDT), total score = (1- 6): a high score reflected more impairment of cognitive function, while a score of 1-2 was considered normal.

1= prefect, 2= minor visuospatial error (minor abnormal spacing and orientations of numbers),

3= in accurate representation of time with normal or minor visuospatial error.

4= Moderated visuospatial error (poor spacing, reverse number orientation, continues number after 12,13,14, unable to write numbers accurately).

5= sever disorganization as described in score 4. 6= no reasonable representation of the clock.

3 **Manos and WU method.[**12]

The clock is divided into eighths partition, beginning with a line through the number 12 and the center of the circle if the 12 is missing

One point each is given for the numbers 1, 2, 4, 5, 7, 8, 10, and 11 if at least half the area of the number is in the proper octant of the circle relative to the number 12.

One point each is given for an obvious short hand pointing at the 11 and an obvious long hand pointing to the 2. The difference in the length of the hands must be obvious at a glance. Total score = (0-10), with a low score reflecting more cognitive function impairment. 10 suggests that cognitive impairment (CI) is unlikely.

Follow-up:

Two months later, 2D-echocardiography were repeated with cognitive function tests. We assessed the presence and degree of remodelling (LVEDV, LVESV by biplane Simpson's method), the presence and degree of EF change by biplane Simpson's method, and the degree of change in (cognitive function test results).

we defined LV remodelling as a change of LVEDV and or LVESV equal or ≥15% by biplane Simpson's method, compared with the echocardiographic study performed at the acute stage. We consider that increased LVEDV or ESV ≥15% from baseline means poorer remodelling (adverse remodelling), while decreased LVEDV or ESV ≥15% from baseline means improved remodelling (reverse remodelling), while increased EF ≥10% of the baseline means improved systolic function and decreased EF ≥10% from baseline means poorer EF.

Then we classified patients into four groups:

1 A group of no change and or improved EF.
2 A group of poorer EF.
3 A group of adverse remodelling (poorer LVEDV, LVESV).
4 A group of no change and or improved remodelling (reverse remodelling).

4. Statistical methods:

The IBM 26 version of SPSS (statistical package of social sciences) was used for data entry and statistical analysis. the collected data tabulated then statistically analyzed by

a) Descriptive statistics of obtained variables from 2D- echocardiography and cognitive function in patients were presented as mean, standard deviations, and median according to test of normality and data distribution.
b) Relationship between remodeling and cognitive function test changes was done using the chi-square test and likelihood ratio.
c) Spearman and Pearson Correlation coefficient analysis was used to find a relationship between cognitive function, LV volumes and function.

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d) Roc curve analysis to find prediction abilities of cognitive function, in early prediction of remolding after acute myocardial infarction.

RESULTS:

Demographic & clinical characteristics:

Patient group

26 (78.7%) males to 7 (21.2%) females, with 18 (54.5%) between 50 and 60 years, 5 (15%) above 60 and 10 (30.3%) below 50 years, 21(63.6 %) of patients were smokers. 11 (33.3%) patients were diabetic, 14 (42.4%) patients were hypertensive, and 8 (24.2%) patients had chronic kidney diseases (CKD).

19 (57.5%) patients were anterior MI and the rest represented other MI types (inferior, posterior, lateral and right MI).12 (36.3%) underwent primary percutaneous coronary intervention (PCI), 14 (42.4%) patients received thrombolytic treatment, while 10 (71.4%) of them underwent pharmaco-invasive PCI after that. 6 (18%) patients were presented late with no chest pain within 48 hours, but with heart failure (HF) symptoms, while about (83.3%) of them had CKD.

There was non-normal distribution in most variable data and normal distribution in some variables, with average means and medians as shown in the following tables. (Tables 1,2).

TABLE 1: Descriptive statistics of patient variables at the acute STEMI stage by 2D echocardiography, cognitive function test results.

VARIABLES AT THE ACUTE STAGE	number	MEAN +/- STANDER DEVIATION (SD)	MEDIAN	TEST SIGNIFICANCE P-VALUE
AGE	33	53,6y r+/-11		.585
LV ESV	33		33ml	.006
LV EDV	33		55ml	.007
LV EF	33	41% +/-7.8		.23
LV EF2-chamber	33	43.12% +/-10.8		.676
LV EF4-chamber	33	40.12% +/-8		.609
Mini-cog test score	33		3	.023

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Manos-cognitive function test score	33		4	.002
Shulman-cognitive function test score	33		3	.000

TABLE 1: Illustrated means and median of LV (ESV EDV EF) and Cognitive test **at** acute STEMI. EDV (end-diastolic volume), ESV (end-systolic volume), EF (ejection fraction), LV (left ventricle), STEMI (ST elevation myocardial infarction).

TABLE 2: Descriptive statistics of patient variables at the follow up 2-month post STEMI stage by 2D echocardiography, cognitive function tests.

VARIABLES AT FOLLOW-UP	**Number**	**MEAN +/- stander deviation (SD)**	**MEDIAN**	**TEST SIGNIFICANCE P-VALUE**
LV ESV	19		25ml	.000
LV EDV	19		48ml	.017
LV EF	19	45% +/-10.5		.080
EF2-Chamber	19	41,7% +/-14.7		.205
EF4-Chamber	19		50%	.010
Mini- cog test score	21		3	.009
Manos cognitive function score	21		8	.000
Shulman-cognitive function score	21		2	.000

TABLE 2: variables for patients at follow-up 2 months post STEMI by 2D echocardiography, and cognitive function test. Illustrated mean and median of (ESV EDV EF) and Cognitive test. EDV (end-diastolic volume), ESV (end-systolic volume), EF (ejection fraction**), LV** (left ventricle**).** STEMI (ST elevation myocardial infarction)

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Control group

About 8 (30.7%) were females and 18 (69.2%) males. 9 (34.6%) were aged between 50 and 60 years, while 6 (23%) were more than 60 years and 11(42.3%) were less than 50 years. 14 (53.8%) were smokers, 7 (26.9%) were diabetic and 5 (19.2%) hypertensives. There was no statistically significant difference between case and control regarding age, sex and smoking behaviour.

There was a statistically significant difference in means between the case group in acute presentation and the control group, which was assessed by non-parametric independent tests (Mann-Whitney U and Wilcoxon W test).

- There were significant differences in cognitive function (Mini-cog and Shulman methods for assessing the clock drawing test), LV dimensions and volumes (ESV, EF, EF, EF 4-chambers, EF 2-chambers by biplane Simpson's method).

There was also a statistically significant difference in means between the case group in the follow-up (2-month post-MI) and the control group

- The significant difference in cognitive function (Shulman, Manos cognitive function tests), and LV function (EF, EF 4 chambers and EF 2 chambers).

Remodelling results:

Adverse remodelling occurred in 7 (31.8%) patients, 3/7 (42.8%) had an increase in ESV and 7/7 (100%) patients had increased EDV.

There was reverse remodelling in 13 (59%) cases, about 10/13 (79.9%) had a decrease of EDV and 12/13 (92%) patients had a decrease in ESV.

- There was a significant relationship between LV remodelling that occurred 2 months post-MI and a change in cognitive function.
- There was a significant relationship between a change in LV (ESV, EDV, EF by biplane Simpson's method), and cognitive function This is all based on an assessment using the chi-square test.

There was a relationship between cognitive function LV volumes, and EF.

1- The Shulman method for CDT assessment of cognitive function in the acute stage correlated with EF_2 chambers by biplane Simpson's method. (The higher score means poor cognitive function and associated with impaired EF). **Spearman correlation (r -0.351, p-value 0.045).**

2- The Shulman method for assessing cognitive function at the follow-up stage correlated with an increase in EF, and EDV in the follow-up stage. **Spearman correlation (r -0.675, p-value 0.023, r -0.476, p-value 0.034 respectively).**

3- Mini-cog method for CDT assessment of the cognitive function in the acute stage (the higher score means good cognitive function) correlated with the degree of increase in EF by biplane Simpson's method at follow -up. **Spearman correlation (r +0.683, p-value 0.021,).**

4- The degree of increase in the Mini-cog method for the clock drawing test score of the cognitive function correlated with the degree of increase in 2-chambers EF **Spearman correlation (r+1.00, p value < .000).**

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5- Manos method CDT for assessing cognitive function in the follow-up stage (the higher score means good cognitive function) correlated with EDV by biplane Simpson's method at the follow-up. **Spearman correlation (r +0.532, p-value 0.016)**

6- The degree of increase in Manos cognitive function, correlated with EDV by biplane Simpson's method at the follow-up. **Spearman correlation (r +0.533 p-value 0.023).** (Table 3).

TABLE 3: Correlation of cognitive function with LV volume (EDV) and EF, and EF change

LV variables in STEMI	Shulman CDT in the acute stage	Shulman CDT in follow up	Mini-cog CDT in the acute stage	Manos CDT in follow up	increase Mini-cog CDT	Increase Manos CDT
EF2 chambers in acute stage	r= - 0.351 p-value 0.045					
EF 2 chambers at follow up.					r=+0.492 p-value 0.032	
Degree of increase EF		r=- 0.675 p-value 0.023	r=+0.683 p-value 0.021			
EDV in the follow up		r=- 0.47 P value 0.34		r=+0.532 p-value 0.016		r=+0.533 p-value 0.023

TABLE 3: illustrated correlation of cognitive function with LV EDV and EF in acute STEMI stage and at 2 months later, and increase in EF at follow up. CDT (clock drawing test), EDV (end-diastolic volume), EF (ejection fraction), LV (left ventricle). STEMI (ST elevation myocardial infarction)

Correlation Relationship of cognitive function and LV post STEMI

Correlation between cognitive function and EF (decreased EF associated with impaired cognitive function)

Shulman cognitive test in the acute stage correlated with EF and in the follow-up also correlated with the increase in EF by Simpson's method. This means there is a connection between decreased EF and impaired

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cognitive function. Mini-cog cognitive test in the acute stage correlated with the degree of increase in EF and the degree of increase Mini-cog cognitive test also correlated with EF in the follow-up stage (an increase in EF associated with an increase in cognitive function performance).

Correlation between cognitive function and LV volumes: Shulman and Manos cognitive test in the follow-up correlated with EDV, as an increase cognitive function performance associated with an increase EDV.

From our correlation data we can say that:

- Cognitive function at first assessment has a positive relationship with EF months post-MI.

BY ROC CURVE ANALYSIS

It was surprising that cognitive function assessment in acute STEMI produced a very acceptable predictor for an improvement of LV volumes, and decline of LV systolic function. (Table 4, figure 1).

The AUC:

Cognitive function in the acute stage of STEMI can be accepted as a predictor of a decrease EF and improvement in EDV, ESV.

- Mini-cog test for cognitive function assessment can be a predictor of a decrease in EF using the biplane Simpson's method with best cut-offs *(3.5/5 score, AUC 0.73).*
- The Manos method for cognitive function assessment could be a predictor of an improvement in ESV using the biplane Simpson's method after 2 months, with best cut-offs *(6.5/10 score, AUC 0.62, 6.5/10score, AUC 0.68 respectively).*
- The Mini-cog test for cognitive function assessment could predict an improvement in ESV, EDV using the biplane Simpson's method 2 months later with the best cut-offs *(2.5/5 score, AUC 0.63, 2.5/5 score, AUC 0.60 respectively).*

TABLE 4: ROC curve analaysis with area under curve for cognitive function for predection LV remodeling and EF post MI

	Mini-cog cognitive function with Area under curve (AUC)	**Cut-offs**	**Manos cognitive function**	**Cut-offs**
worsen EF	AUC .737	3.5/5 score Sensitivity 50% specificity 96%		
Reverse			AUC	6.5/10

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remodeling biplane Simpson's method			.602	score Sensitivity46 % specificity 75%
Improved EDV	AUC .600	2.5/5 score Sensitivity70% specificity 53%		
Improved ESV	AUC .637	2.5 /5score Sensitivity55% specificity 65%	AUC .685	6.5/10 score Sensitivity53 % specificity 80%

TABLE 4: illiusterated areas under the curve with estimated cut-off point with corresponding sensitivity and specificity of improved EDV, ESV and decrease in EF. EDV (end-diastolic volume), ESV (end-systolic volume), EF (ejection fraction), LV (left ventricle).MI (myocardial infarction)

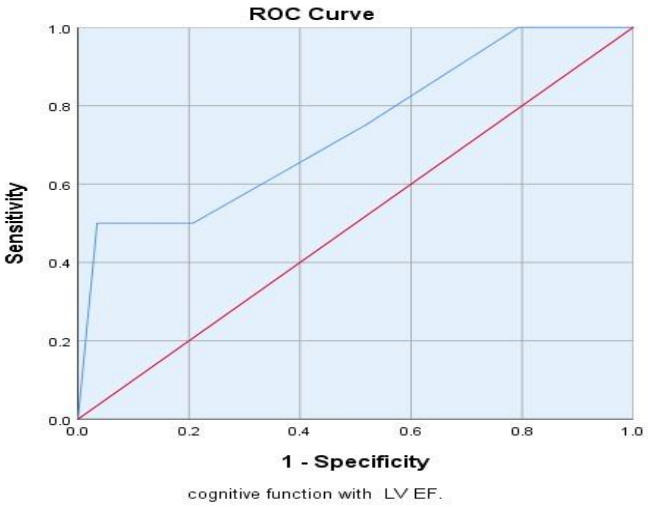

Fig 1: ROC curve for cognitive function prediction ability of decreases LV EF area under curve AUC (0.737).

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Discussion

In the present study, we tested the relationship between cognitive function and LV post STEMI and tested the ability of cognitive function for predicting LV post-STEMI remodelling. We defined remodelling as a change in LVEDV and or LVESV of ≥15% 2-months post- STEMI, and EF changes by Simpson's method ≥10% compared with the echocardiographic study performed at the acute stage by Simpson's method (increasing or decreasing). We are concordance with Systematic literature research, using MEDLINE and the Cochrane Library from January 2010 to August 2019, it concluded that the most frequent LVR (left ventricular remodeling) criterion was a 20% increase in end-diastolic volumes or a 15% increase in end-systolic volumes using follow-up CMR imaging 3 months after STEMI. [14]. Many different tests were used in literature for assessing the Cognitive function, the clock drawing test (CDT), Mini-cog test, Mini-cog-Mental State Examination. The clock drawing test (CDT) was considered as rapid and easy way for assessing the cognitive function. that simple CDT scoring systems are sufficient for differentiating patients with mild cognitive impairment and mild dementia from normal cognitive function.[15]. The Mini- Cog is effective as or better than established screening tests in both an epidemiologic survey in a mainstream sample and a multi-ethnic, multilingual population comprising many individuals of low socioeconomic status and education level. In comparative tests. The Mini- Cog is less affected by subject ethnicity, language, and education, and can detect a variety of different dementias.[15]. For that we choose CDT in evaluation with different scoring methods (Mini-cog, Shulman, and Manos and Waston et al) to be sure from our evaluation.

specialists in meta-analysis suggest that coronary heart disease is associated with increased odds of developing cognitive impairment or dementia [8]. This is of great concern, given the projected worldwide increase in the number of people affected by coronary heart diseases and dementia. [8]. Cognitive function associated with ischemic heart diseases [8] and HF [2-7] and HTN [16]. Many different mechanisms can be considered to be a cause of the relationship between heart diseases and cognitive function like sharing risk factors of the cardiovascular diseases and cerebrovascular diseases, affection of blood supply to brain due to heart diseases, possibility of micro cardiac emboli, change in neurotransmitter like sympathetic and parasympathetic changes, acetylcholine level change, endothelial dysfunction.

In the present study, we found a significant relationship between the cognitive function change and remodelling that occurs 2 months after MI, and a significant relationship with change in EF, ESV, and EDV that forced by correlation of cognitive function with LV EF. Cognitive function in the acute stage of STEMI can be accepted as a predictor of a decrease EF and improvement in EDV, ESV 2- months later.

Summary

There is a relation between heart and cognitive function. We found that cognitive function had a relation with LV remodelling and LV systolic function. As a good EF associated with good cognitive function performance in 33 STEMI patient threw a case control observational study in Aswan university hospital between November 2020 and May 2021 in the acute stage and at 2-months follow up stage. Also increase EF post-STEMI associated with good cognitive function in the acute and follow up stages and increase cognitive function strongly associated with increase EF.

We tried to find if cognitive function affected early by change in LV volume and function post-STEMI by tested its prediction ability of LV remodelling post STEMI, we found that:

- Cognitive function in the acute stage of STEMI can be accepted as a predictor of a decrease EF using the biplane Simpson's method 2 months later.
- Cognitive function in the acute stage of STEMI can be accepted as a predictor of improvement in EDV, ESV using the biplane Simpson's method 2 months later.
- May use the Cognitive function as a new simple method for predicting LV remodelling and EF post-STEMI to direct us for more evaluation of cardiac remodeling post STEMI

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That raised aquations about what are possible mechanisms make that relations???

Conclusion:

- The cognitive function had a relation with LV remodelling and LV systolic function post-STEMI. As a good EF associated with good cognitive function performance in the acute stage and at two-months post-STEMI
- Cognitive function can be a predictor of reverse LV remodelling and EF change at the tow-month post-STEMI stage.

Conflicts of interest

The authors declare no potential conflicts of interest.

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