CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

The Relationship between Epicardial Adipose Tissue Thickness and Cardiovascular Risk Factors

Association entre l'épaisseur du tissu adipeux épicardique et les facteurs de risque cardiovasculaire

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Summary

Introduction: Previous studies have indicated that epicardial adipose tissue (EAT) may predict obstructive coronary artery disease (CAD). We aimed to assess the correlation between common cardiovascular risk factors and EAT.

Methods: This was a prospective, descriptive and analytic study that included 100 consecutive patients admitted to the cardiology department for coronary angiography between November 2020 and April 2021. Patients were interviewed regarding conventional coronary risk factors, provided blood samples and underwent transthoracic echocardiography to measure EAT thickness.

Results: The mean age was 58±12 years, with a masculine predominance (sex ratio= 6.14). The mean values of end-diastolic EAT (ED.EAT) and end-systolic EAT (ES.EAT) were 3.38±0.88 mm and 5.17±1.34 mm, respectively. ED.EAT and ES.EAT were positively correlated with age (r=0.485, p<0.001; r=0.397, p<0.001, respectively). Smoking patients had higher ED.EAT (3.16±0.83 vs 3.58±0.89, p=0.016) while both, ED.EAT and ES.EAT were significantly higher in diabetic patients (3.59±0.86 vs 3.12±0.85, p=0.008 and 5.47±1.39 vs 4.79±1.17 p=0.011, respectively), in dyslipidemic patients (3.47±0.87 vs 2.79±0.77, p=0.008 and 5.29±1.34 vs 4.42±1.1, p=0.025, respectively) and in patients with overweight/obesity (2.9±0.8 vs 3.5±0.8, p=0.018 and 4.6±1.3 vs 5.3±1.3, p=0.049, respectively). There was no correlation between EAT thickness and either hypertension or sex. Among the biological parameters, ES.EAT was negatively correlated with high-density lipoprotein cholesterol (r=-0.234, p= 0.02), while no significant correlation was found with the other biological parameters.

Conclusion: EAT and CAD share most cardiovascular risk factors, which supports the potential role of EAT in cardiovascular risk assessment.

Keywords

epicardial adipose tissue, cardiovascular risk factors, echocardiography

Résumé

Introduction : Des études précédentes ont indiqué que le tissu adipeux épicardique (EAT) peut prédire une maladie coronarienne obstructive. Le but de notre travail est d'évaluer la corrélation entre les facteurs de risque cardiovasculaire classiques et le tissu adipeux épicardique.

Méthodes : Il s'agit d'une étude prospective, descriptive et analytique qui a inclus 100 patients consécutifs admis au service de cardiologie pour une coronarographie entre novembre 2020 et avril 2021. Les patients ont été interrogés sur les facteurs de risque cardiovasculaires classiques, ont eu un bilan biologique et une échocardiographie transthoracique pour mesurer l'épaisseur de l'EAT.

Résultats : L'âge moyen était de 58±12 ans, avec une prédominance masculine (sex-ratio= 6.14). Les valeurs moyennes de l'EAT en fin de diastole (ED.EAT) et de l'EAT en fin de systole (ES.EAT) étaient respectivement de 3.38±0.88 mm et de 5.17±1.34 mm. L'ED.EAT et l'ES.EAT étaient positivement corrélées avec l'âge (r=0,485, p<0,001 ; r=0,397, p<0,001, respectivement). Les patients fumeurs avaient une ED.EAT plus élevée (3.16±0.83 vs 3.58±0.89, p=0.016) alors que l'ED.EAT et l'ES.EAT étaient significativement plus élevées chez les patients diabétiques (3.59±0.86 vs 3.12±0.85, p=0.008 et 5.47±1.39 vs 4.79±1.17 p=0. 011, respectivement), chez les patients dyslipidémiques (3.47±0.87 vs 2.79±0.77, p=0.008 et 5.29±1.34 vs 4.42±1.1, p=0.025, respectivement) et chez les patients en surpoids/obésité (2.9±0.8 vs 3.5±0.8, p=0.018 et 4.6±1.3 vs 5.3±1.3, p=0.049 ; respectivement). Il n'y avait pas de corrélation entre l'épaisseur de l'EAT et l'hypertension ou le sexe. Parmi les paramètres biologiques, l'ES.EAT était négativement corrélé avec le HDL cholestérol (r=-0.234, p=0.02), alors qu'aucune corrélation significative n'a été trouvée avec les autres paramètres biologiques.

Conclusion : L'EAT et la maladie coronarienne partagent la plupart des facteurs de risque cardiovasculaire, ce qui confirme le rôle potentiel de l'EAT dans l'évaluation du risque cardiovasculaire

Mots-clés

Tissu adipeux épicardique, facteurs de risque cardiovasculaire, échocardiographie

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INTRODUCTION

Multiple cardiovascular risk factors contribute to the development of coronary atherosclerosis, with obesity being one of them. Obesity is defined by the World Health Organization as an abnormal or excessive accumulation of body fat that can be detrimental to health(1). Some of these deposits could contribute to the cardiovascular risk, including epicardial adipose tissue (EAT). EAT is the true adipose tissue of the heart, it is located between the myocardium and the visceral layer of the pericardium (2).

Several studies have clearly established a close relationship between EAT and coronary artery disease (CAD) (3–8). Thus, measurement of EAT thickness has gained importance and has become a common practice to predict obstructive coronary artery disease. EAT thickness can be measured by transthoracic echocardiography, cardiac computed tomography (CT), and cardiac magnetic resonance imaging (MRI) methods (9).

Although CT and MRI have better image quality and can perform volumetric measurements, they are limited by high costs, low accessibility and complexity of measurement. Transthoracic echocardiography has advantages over CT and MRI, such as easy availability, low cost, no radiation exposure, rapidity and high reproducibility.

Thus, EAT might represent a novel parameter that is inexpensive and easy to obtain and may be helpful in cardiovascular risk stratification and in primary prevention for people who are at high risk for acquiring CAD.

In our study, we aimed to assess the correlation between common cardiovascular risk factors and EAT thichness.

METHODS

Study population

We prospectively enrolled 100 consecutive patients aged more than 30 years old admitted to the cardiology department for coronary angiography between November 2020 and April 2021. Non-consenting patients to participate in the study or those with a history of cardiac surgery (coronary artery bypass grafting or valve replacement) were not included. Patients with poor echogenicity were excluded from the study. The hospital's ethics committee approved the study. Informed verbal consent was obtained from all patients before their participation.

Patients were interviewed regarding the presence of conventional coronary risk factors (diabetes mellitus, hyperlipidaemia, hypertension, smoking, and a family history of CAD). Height, waist circumference (WC) and weight were measured during hospitalisation.

WC was measured at the umbilicus.

Body mass index was calculated as body weight divided by the square of height.

Blood samples were obtained during fasting, and levels of plasma glucose, Glycated haemoglobin, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides were measured.

Hypertension was defined as systolic blood pressure > 140 mm Hg and/or diastolic pressure > 90 mm Hg or current treatment with antihypertensive medication.

Diabetes was defined as fasting blood glucose > 200 mg/dl, glycated haemoglobin 6.5%, and/or the need for oral hypoglycaemic agents or insulin.

Dyslipidaemia was defined as plasma total cholesterol > 220 mg/dl or the use of lipid-lowering therapy.

Smoking was defined as current or previous use of cigarettes.

Family history of premature coronary heart disease was defined as the occurrence of a fatal or non-fatal myocardial infarction and/or coronary angioplasty/ coronary artery bypass surgery before the age 55 years in a first degree male relatives or the age 65 years in a first degree female relatives (10) .

Echocardiographic Examination

All patients underwent Transthoracic echocardiography with a Philips EPIQ 7 (Philips Medical Systems, Andover, MA, USA) with a 5S1 transducer.

EAT thickness is measured between the epicardium of the right ventricle and parietal pericardium.

For EAT thickness measurement, patients were placed in the left lateral decubitus position. A parasternal long-axis view was obtained through the left sternal 2-3 intercostal space. EAT thickness consists of measuring vertically the hypoechoic area extending from epicardial surface to the parietal

pericardium in front of the right ventricular free wall at the thickest level in three cardiac cycles during end-systole and end-diastole using both M and 2 dimensional modes (Fig 1 A, Fig 2B).

After measuring from the parasternal long-axis, parasternal short axis view is obtained by switching to 90° clockwise. EAT thickness is measured from the hypoechoic area between the right ventricle and parietal pericardium in three cardiac cycles during end-systole and end-diastole using both M and 2 dimensional modes (Fig 1B, Fig2B).

The average of Parasternal long-axis and short-axis measurements is calculated to obtain the mean thickness: end diastolic EAT (ED-EAT) and end systolic EAT (ES-EAT) thickness.

STATISTICAL ANALYSIS

The data were analyzed using SPSS software version 25. Simple frequencies and percentages were calculated for qualitative variables, while means and standard deviations were determined for quantitative variables. Student's t-test was used to compare two means on independent series, and one-way ANOVA analysis was employed for comparing three means. Pearson's chi-square test was utilized for comparing percentages. Pearson's correlation coefficient (R) was estimated to study the correlation between two quantitative variables.

RESULTS

The study population consisted of 100 patients, the mean age was 58±12 years, with a masculine predominance (86% male vs 14% female with a sex ratio of 6.14).

Hyperlipidaemia was the most frequent cardiovascular disease risk factors (86%) followed by hypertension (57%) and diabetes (57%).

Patient characteristics are presented in Tables 1.

Correlation of end systolic and end diastolic EAT thickness with different variables were analysed in the tables 2 and 3.

ED.EAT thickness was significantly correlated with smoking (p=0.016).

Table 1. Baseline characteristics of the study population

Age		Mean measures
Weight		85.93±15.82
Size		172.13±9.01
Waist circumference	Male	103.73±13.26
	Female	105.36±13.98
Body mass index		28.76±5.20
Systolic blood Pressure		131.5±22.11
Diastolic blood pressure		73.9±10.14
Heart rate(bpm)		81±19.77
Fasting blood Glucose (g/l)		1.23±0.47
HBA1c (%)		7.1±1..99
Total cholesterol (g/l)		1.61±0.40
Triglycerides (g/l)		1.40±0.80
HDL cholesterol (g/l)		0.36±0.09
LDL cholesterol (g/l)		0.94±0.32
Hb (g/dl)		13.37±1.7
Creatinine (µmol/L)		97±112
ED.EAT thickness (mm)		3.38±0.88
ES.EAT thickness (mm)		5.17±1.34

bpm: beat per minute ; ED.EAT: End diastolic epicardial adipose tissue ; ES.EAT: end systolic epicardial adipose tissue; LDL: low density lipoproteins; HDL: high density lipoproteins; HbA1C: glycated haemoglobin; Hb: haemoglobin.

Table 2. EAT thickness according to cardiovascular risk factors.

		ED.EAT thickness	ES.EAT thickness
Gender	Male (n=86)	3.38±0.85	5.22±1.31
	Female (n=14)	3.37±1.08	4.85±1.49
	p	0.979	0.340
Diabetes	Yes (n=55)	3.59±0.86	5.47±1.39
	No (n=45)	3.12±0.85	4.79±1.17
	p	0.008	0.011
Hypertension	Yes (n=57)	3.51±0.82	5.27±1.28
	No(n=43)	3.20±0.93	5.02±1.41
	p	0.79	0.354
Dyslipidaemia	Yes (n=86)	3.47±0.87	5.29±1.34
	No (n=14)	2.79±0.77	4.42±1.10
	P	0.008	0.025
Smoking	Yes(n=49)	3.16±0.83	4.97±1.3
	No(n=51)	3.58±0.89	5.35±1.36
	p	0.016	0.15
Family History of premature CAD	Yes(n=15)	3.09±0.92	4.77±1.37
	No(n=85)	3.43±0.87	5.24±1.33
	p	0.22	0.2

ED.EAT: End diastolic epicardial adipose tissue ; ES.EAT: end systolic epicardial adipose tissue ; CAD: coronary heart disease

Table 3. Clinical and laboratory characteristics population according to EAT thickness.

Parameters	ED.EAT thickness thickness		ES.EAT thickness	
	r	P	R	P
Age	0,525	<0,001	0,419	<0,001
Weight	0,016	0,875	0,084	0,407
Size	-0,327	0,001	-0,233	0,02
Waist circumference	0,255	0,011	0,311	0,002
Body mass index	0,192	0,056	0,21	0,036
Systolic blood Pressure	0,148	0,143	0,216	0,031
Fasting blood Glucose	0,151	0,15	0,168	0,107
HBA1c	0,07	0,08	0,09	0,14
Total cholesterol	-0,016	0,872	-0,027	0,789
Triglycerides	0,146	0,15	0,151	0,137
HDL cholesterol	-0,187	0,063	-0,234	0,02
LDL cholesterol	-0,036	0,727	-0,038	0,71

HDL, high-density lipoprotein; LDL, low-density lipoprotein; HBA1c: glycated haemoglobin
ED.EAT: end diastolic Epicardial adipose Tissue; ES.EAT: end systolic Epicardial adipose Tissue

DISCUSSION

The key findings of the present study are summarized as follows:

- ED.EAT and ES.EAT were positively correlated with age.
- Smoking patients had higher ED.EAT thickness, and both ED.EAT and ES.EAT were significantly higher in diabetic patients, dyslipidemic patients, and patients with overweight or obesity.
- There was no correlation between EAT thickness and either hypertension or sex.
- Regarding biological parameters, ES.EAT was negatively correlated with high-density lipoprotein cholesterol, while no significant correlation was found with the other biological parameters.

EAT is an unusual visceral fat deposit which is commonly located between the visceral pericardium and the myocardium. It's anatomically, morphologically and functionally different from other fat depots. It supplies energy and heat to the myocardium and exerts a protective role (11). But in the other hand, it turned out that the epicardial fat is a metabolically active organ that secretes inflammatory cytokines such as interleukin-1, interleukin-6, tumor necrosis factor, and monocyte chemotactic protein that affect cardiac function and contribute to the development of coronary artery disease (2,12,13). Iacobellis et al. found that in patients with CAD Adiponectin levels are lower in epicardial tissue than in subcutaneous fat, Adiponectin decreases insulin resistance and has a protective role in the formation of atherosclerosis (13,14).

In our study, EAT thickness consists of measuring vertically the hypoechoic area extending from epicardial surface to the parietal pericardium in front of the right ventricular free wall at the thickest level in three cardiac cycles. Some references recommend the measurements to be made in six (15) and some references recommend to be made in ten (16). Kamal et al(3). measured not only EAT thickness but also horizontal width, and area on the free wall of the right ventricle from the parasternal long axis view and found similar results.

However, echocardiography may not be accurate enough to allow the assessment of the EAT thickness. This is due to its 3-dimensional shape and it is heterogeneous distribution over the heart. Indeed, CT and MRI have better image quality and can perform volumetric measurements. In fact, Aydin et al (7). and Picard et al (17) used CT to measure EAT thickness and proved that patients with CAD had significantly higher EAT than patients without CAD, Liu et al (18) has also used the CT and measured EAT volume in a large population of 617 patients to conclude that the EAT volume was a better predictor of early stage CAD than simple thickness measurements.

Yet widespread use of these methods is not practical due to their high cost and low accessibility. Many studies suggest that echograpcardiographic measurement of EAT thickness was easily reproducible and showed a good correlation with measurements with MRI (3,7,9,19).

In our study, ED.EAT and ES.EAT were positively correlated with age and waist circumference but there was no correlation between either ED.EAT and ES.EAT thickness and sex.

In fact, there is no consensus in the literature on the impact of gender on the epicardial adiposite. Based on the Framingham cohort some authors like Rosito et al (20) suggest that the correlation between EAT and cardiovascular disease risk factors in women is stronger than in men while others studies from the same cohort

did not find any correlation (21,22).

ES.EAT thickness was found to have a statistically significant correlation to body mass index, systolic blood pressure and high density lipoproteins cholesterol.

Verma et al (4) found that EAT thickness was only correlated with waist circumference and LDL cholesterol. In fact, in their study there was no correlation with age weight, body mass index, blood pressure and diabetes.

Unlike kamal et al (3) who found a significant correlation between EAT thickness and many parameters such as age, body mass index, blood pressure, diabetes smoking and dyslipidaemia.

A positive correlation between EAT thickness and age has been noticed in many study cases (23–25). Beside according to some authors thickness tends to increase with age, and this increase is more important in women without any gender association. According to abbara et al EAT thickness seems to increase with age being 22% thicker in people older than 65 years (26).

Since epicardial adipose tissue has the same origin as visceral adipose like we mentioned above, the causality relationship between obesity and increased epicardial fat seems obvious.

In our study only ED.EAT was significantly correlated with body mass index (p=0.036). Iacobbelis et al went to prove that EAT thickness in subjects with metabolic syndrome is higher than that observed in subjects without this syndrome and that waist circumference and fasting insulin were the strongest independent variables correlated with EAT (p=0.02 and p=0.03 respectively) (27).

Aitken-Buck et al (28) compared EAT thickness measured from the parasternal long-axis view in 3 groups of subjects. The first group had normal body mass index the second had overweight and the third had obesity, he noticed that EAT thickness was much more important in the third group compared to the other groups. In fact, EAT thickness was 58.7% greater (p=0.003) in patients from the obese compared to normal category. He concluded to a significant correlation between body mass index and EAT ($r = 0.56$, $p < 0.0001$).

In another study, Willens et al examined the effects of weight loss after bariatric surgery in 23 patients suffering from severe obesity on EAT. Echocardiograms were recorded before and 8.3±3.7 months after undergoing surgery. At baseline, patients had increased epicardial fat compared with normal-weight controls matched for age, gender, and ethnicity (5.3 ± 2.4 vs 3.0 ± 1.1 mm, p <0. 001), Patients lost an average of 40 ± 14 kg after surgery. EAT thickness decreased from 5.3 ± 2.4 to 4.0 ±1.6 mm (p = 0.001)(29)

Many other authors have also demonstrated an association between EAT and several pathologies.

Guan et al (30) showed that hypertensive patients tend to present a higher EAT thickness and that increased EAT thickness can be associated with high risk of non-dipper blood threw his meta-analysis including 14 studies with a total of 2722 subjects.

Similar results to the ones presented in our study were reported by Li et al (31) with 1102 patients included in their study in his meta-analysis. He aimed to show that EAT was thicker in diabetic patients compared to non-diabetics patients. Same for Baldasseroni et al (32) with only 114 patients.

In our study ES.EAT was negatively correlated with high-density lipoprotein cholesterol (r=-0.234, p=0.02) while no significant correlation was found with Low-density cholesterol, total cholesterol and triglycerides.

Similar results to the ones presented in our study were reported by picard et al (17), with 970 patients included in their study , EAT measured by computed tomography was correlated with HDL cholesterol (p=0.02) while there was no significant correlation between EAT and both LDL cholesterol and total cholesterol.

In another study with 150 patient includes Eroglu et al (25) found that EAT thickness correlated with fasting glucose (P=0.044), HDL- cholesterol (P=0.045) and triglycerides (P=0.001) while there was no correlation with total cholesterol and LDL cholesterol.

The lack of correlation between EAT thickness and biological parameters such as LDL cholesterol, total cholesterol, and triglycerides may be explained by the high prevalence of statin use. In fact, 41 patients (41%) in our population were using statins, 38 (38%) of whom had been on them for more than a year. Similarly, the absence of correlation with glycated hemoglobin and fasting blood glucose may be due to the fact that patients were well controlled on antidiabetic treatment.

Study limitations

The present study has several limitations. First, it was a monocentric study with a relatively small sample size, as it was conducted at a single center and included only 100 patients. The second limitation is

that the echocardiograms were performed by two different operators, and inter- and intra-observer variability was not taken into consideration.

CONCLUSION

In a world where coronary artery disease is one of the most common forms of heart disease and a serious global health issue, primary prevention is crucial. Among traditional predictors of CAD, epicardial adipose tissue thickness has emerged as an independent and strong risk factor. In fact, EAT and CAD share many cardiovascular risk factors, which enhances the role of EAT in cardiovascular risk assessment.

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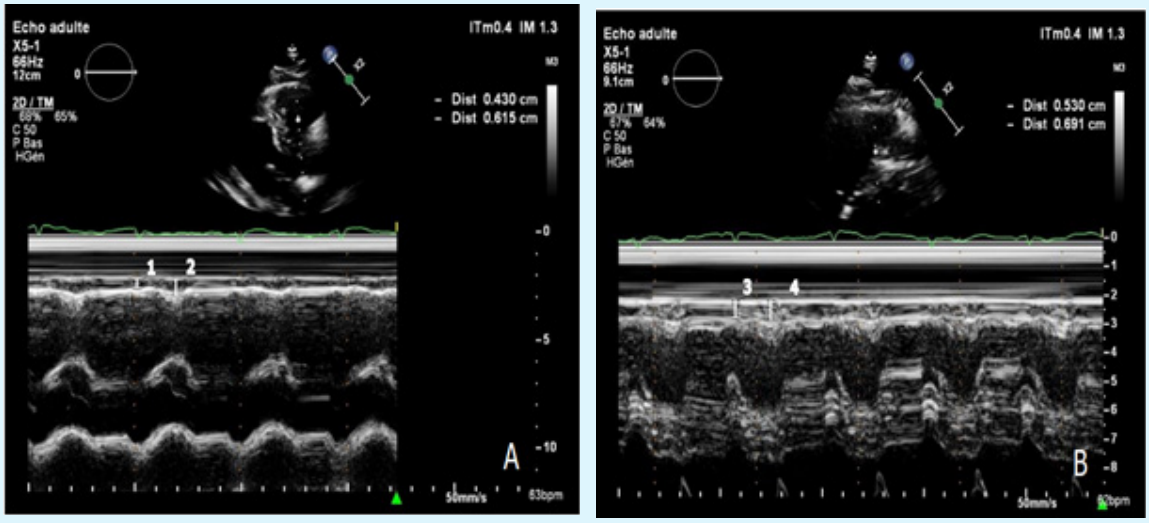

Figure 1A. 1:End diastolic measure of epicardial adipose tissue in long axis view using TM mode 2: End systolic measure of epicardial adipose tissue in long axis view using TM mode. Figure 1B; 1: End diastolic measure of epicardial adipose tissue in short axis view using TM mode 2: End systolic measure of epicardial adipose tissue in short axis view using TM mode.

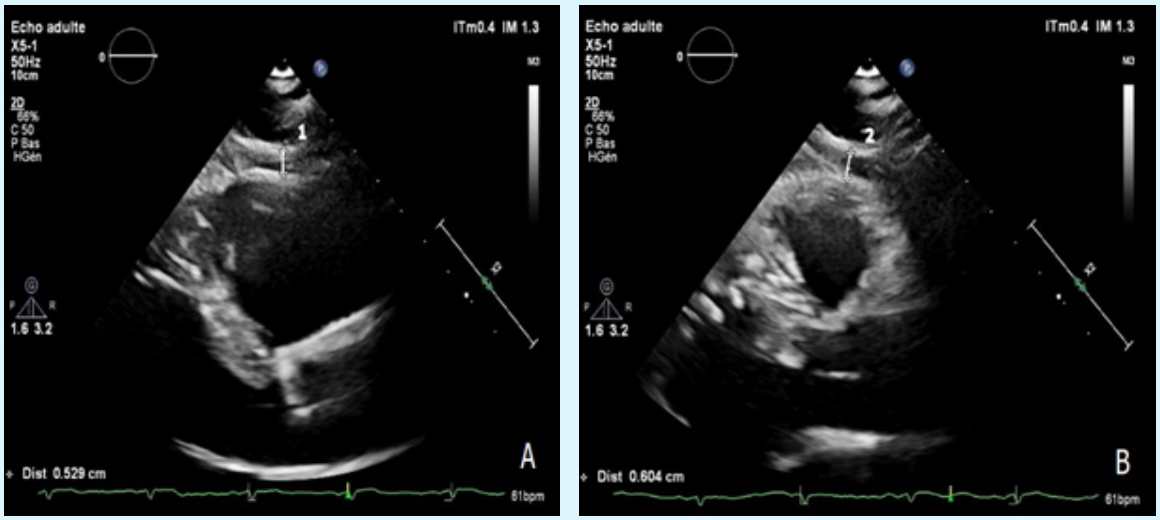

Figure 2A. End diastolic measure of epicardial adipose tissue in long axis view using 2D mode Figure 2B: End systolic measure of epicardial adipose tissue in long axis view using 2D mode.

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