

## ORIGINAL ARTICLE

### ISCHEMIC HEART DISEASE

# Evolution of Systolic Function and Myocardial Perfusion, Evaluated by Gated SPECT, in the First Year after Acute Myocardial Infarction

Jaume Candell-Riera, Osvaldo Perezto-Valdés, Guillermo Oller-Martínez, Joan Llevadot, Santiago Aguadé-Bruix, Joan Castell-Conesa, Marina Soler-Peter, Marc Simó and Jordi Soler-Soler

Servicios de Cardiología y de Medicina Nuclea, Hospital Universitari Vall d'Hebron, Barcelona, Spain

**Introduction and objectives.** Systolic function and myocardial perfusion are evaluated before hospital discharge and can change during follow-up. The purpose of this study was to evaluate these parameters by gated-SPECT in the first year after acute myocardial infarction.

**Patients and method.** We studied 74 consecutive patients with a first uncomplicated acute myocardial infarction (49 infero-lateral and 25 anterior) by stress-rest  $^{99m}\text{Tc}$ -tetrofosmin and rest-gated-SPECT before hospital discharge (6-8 days after admission) and one year after myocardial infarction.

**Results.** The ejection fraction (EF) increased  $> 5\%$  in 51% of infero-lateral infarcts and 28% of non-revascularized anterior infarcts. EF increased significantly ( $48.4 \pm 8\%$  to  $54.6 \pm 8.7\%$ ;  $P < .0001$ , mean difference: 6.2; 95% IC, 2.8-9.5) and systolic volume decreased ( $51.3 \pm 19.2$  ml to  $44.3 \pm 19.4$  ml;  $P = .001$ ; mean diff.: 7.67; 95% IC, 1.5-13.8) in infero-lateral infarctions. The rest perfusion index in the necrotic region improved ( $2.3 \pm 0.57$  to  $2.17 \pm 0.58$ ;  $p = 0.004$ ; mean diff.: 0.18; 95% IC, 0.003-0.36) in infero-lateral infarcts and the ischemia index remained unchanged between the first and second studies.

**Conclusions.** Left ventricular systolic function can change during the first year of evolution, a significant improvement being seen in infero-lateral infarctions. The ejection fraction increased  $> 5\%$  in half of these patients, as opposed to only a quarter of anterior infarctions. This improvement was associated to increased myocardial perfusion at rest.

**Key words:** Myocardial infarction. Scintigraphy. Coronary artery disease. Radionuclides.

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Correspondence: Dr. J. Candell-Riera  
Servicio de Cardiología, Hospital Universitari Vall d'Hebron  
P.º Vall d'Hebron, 119-129, 08035 Barcelona, Spain  
E-mail: [jcandell@hg.vhebron.es](mailto:jcandell@hg.vhebron.es)

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## Evolución de la función sistólica y de la perfusión miocárdica valoradas mediante *gated*-SPECT durante el primer año después de un infarto agudo de miocardio

**Introducción y objetivos.** La función sistólica ventricular izquierda y la perfusión miocárdica pueden experimentar cambios durante el seguimiento y la evolución de un infarto agudo de miocardio. El objetivo de este estudio es su valoración mediante *gated*-SPECT.

**Pacientes y método.** Se ha estudiado a 74 pacientes consecutivos con un primer infarto agudo de miocardio no complicado (49 inferolaterales y 25 anteriores) mediante  $^{99m}\text{Tc}$ -tetrofosmina de esfuerzo-reposo y *gated*-SPECT de reposo antes del alta hospitalaria y al año de evolución.

**Resultados.** Entre el primer y el segundo estudios, la fracción de eyección aumentó  $> 5\%$  en un 51% de los infartos inferolaterales y en un 28% de los infartos anteriores no revascularizados. El aumento de la FE (de  $48,4 \pm 8\%$  a  $54,6 \pm 8,7\%$ ;  $p < 0,0001$ ; diferencia media, 6,2; IC del 95%, 2,8-9,5) y el descenso del volumen sistólico (de  $51,3 \pm 19,2$  ml a  $44,3 \pm 19,4$  ml;  $p = 0,001$ ; diferencia media, 7,67; IC del 95%, 1,5-13,8) alcanzaron valores estadísticamente significativos en los infartos inferolaterales. Los índices de perfusión en reposo en la región del infarto mejoraron entre los dos estudios en los infartos inferiores (de  $2,3 \pm 0,57$  a  $2,17 \pm 0,58$ ;  $p = 0,004$ ; diferencia media, 0,18; IC del 95%, 0,003-0,36), sin cambios en los índices de isquemia.

**Conclusiones.** La función sistólica ventricular izquierda puede cambiar durante el primer año de evolución, mejorando especialmente en los infartos inferolaterales. En la mitad de éstos, pero sólo en una cuarta parte de los anteriores, la fracción de eyección aumentó más de un 5% entre el primer y el segundo estudios. Esta mejoría se asoció a un incremento de la perfusión miocárdica en reposo.

**Palabras clave:** Infarto de miocardio. Gammagrafía. Enfermedad coronaria. Isótopos.

## INTRODUCTION

Left ventricular systolic function and residual ischemia, evaluated before discharge, hospital are important prognostic factors in patients who have suffered an

## ABBREVIATIONS

AMI: acute myocardial infarction  
 EF: ejection fraction  
 SPECT: single photon emission tomography  
 LV: left ventricle

acute myocardial infarction (AMI).<sup>1,2</sup> However, these parameters can change spontaneously over the following months. Experimental studies have shown that myocardial contraction abnormalities following a coronary obstruction are potentially reversible,<sup>3,4</sup> and isotopic ventriculography has been used to follow the changes in ventricular volumes and the ejection fraction (EF) of the left ventricle following AMI.<sup>5-20</sup> Myocardial perfusion tomography synchronized with ECG (gated SPECT) allows stress and resting perfusion to be evaluated, and permits estimations of the ventricular volumes and left ventricular systolic function.<sup>21-24</sup> However, no papers report the use of this technique to monitor these parameters following AMI. The aim of this work was to determine the changes in these parameters in patients who had suffered their first noncomplicated AMI, between the time prior to their release from hospital and one year later.

## PATIENTS AND METHODS

### Study subjects

The study subjects were 74 hospitalized patients (55±9 years of age; 9 women) who had suffered their first noncomplicated AMI, from a total of 196 consecutive patients admitted to the Coronary Unit of our hospital over a period of one year. Forty-one of this larger total were excluded because they had suffered a previous AMI, 34 because they had complications during their stay in hospital, 18 because they had been revascularized (12 by angioplasty and six by surgery) before the second examination, 12 because they refused a second examination at one year, 9 because of serious associated noncardiac disease, 3 because of inadequate gated-SPECT examination, 3 because of a further infarction, and 2 because of death during the first year post-AMI.

### Gated SPECT

Before hospital discharge (6-8 days after admission), and again one year after AMI, the study subjects underwent stress-rest myocardial perfusion 99mTc-tetrofosmin gated-SPECT. The stress-rest test was performed using an ergometric bicycle with an initial load of 50 watts, applying 25-watt increments every 3 min

until the appearance of symptoms, an inadequate blood pressure response or a fall of >0.2 mV in the ST segment. Between 30 and 60 s before finishing the stress test, patients were given an intravenous dose of 99mTc-tetrofosmin (8 mCi). Stress images were obtained 15-30 min later. A second dose of 20-25 mCi was then administered and rest images obtained 30-60 min later. Acquisitions were made with an Elscint SP4 gamma camera equipped with a low-energy, high-resolution collimator. Sixty projections were obtained in step-and-shoot mode for a 180° semicircular orbit, starting at the oblique anterior right position, angled at 30°, and with detection every 3° for 20 s each. In the resting gated SPECT study, 8 images were obtained per projection angle during each cardiac cycle. Images were reconstructed (Butterworth filter, order 5, section frequency 0.4 cycles/pixel), obtaining short, long horizontal and long vertical axis sections.

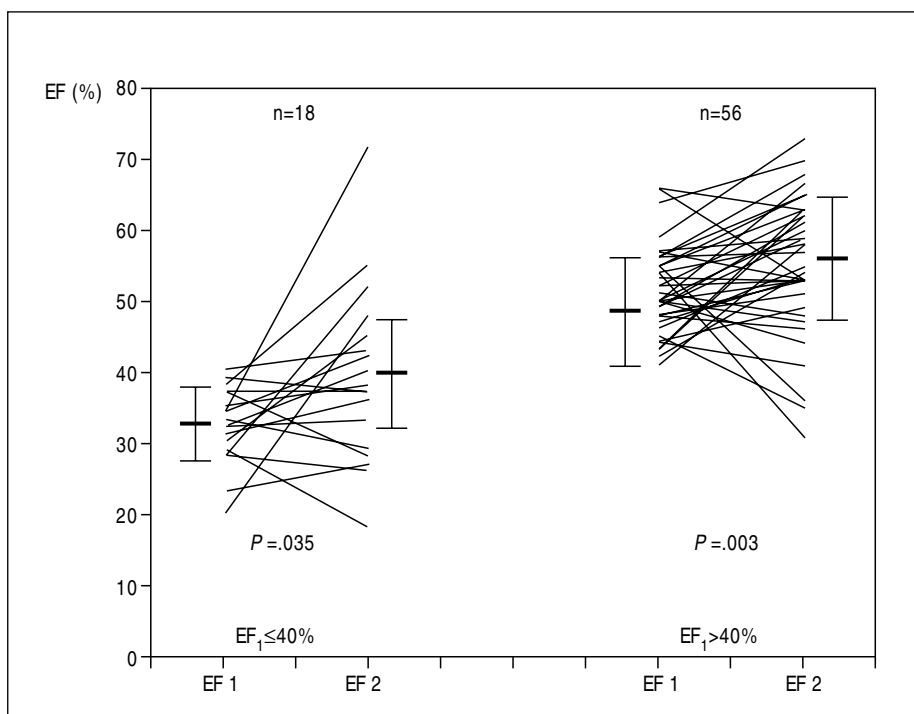
The LV was divided into 20 segments: 6 in the long vertical axis, 6 in the long horizontal axis, 4 in the short basal axis and 4 in the short medial axis. Points were awarded to each (from 1-4) according to the uptake level: 1=normal, 2=slight defect, 3=moderate defect, and 4=important defect. All studies were evaluated by consensus by three expert observers, and the resting perfusion indices (sum of scores at rest/20) and ischemia indices (sum of stress scores–sum of rest scores/20).

From the resting gated SPECT study, the volumes and EF of the LV were calculated using a three-dimensionally-operating automatic quantification algorithm that takes into account the volume of the ventricular cavity in the synchronized images of the short axis.<sup>25</sup>

### Statistical analysis

Comparisons were made between the stress test and scintigraphic values (volumes, EF, resting perfusion index in the infarcted area, and ischemic index) recorded at the first and second examinations for all patients, the subgroups of inferolateral and anterior infarction patients, those who received/did not receive fibrinolytic treatment, and those treated/not treated with angiotensin converting enzyme inhibitors or beta-blockers at the time of the second study. Comparisons were also made between the number of patients requiring treatment with nitrates, calcium antagonists and betablockers at the times of the first and second examinations.

The Chi-squared test was used to compare associations between categorical variables, whereas the Student's t was used test for continuous variables. To analyze changes between the first and second examination, the Student's t test was used for paired data. The differences between means and the 95% confidence intervals for these differences were calculated. Statistical significance was set at 5%. The interobserver variability (dif-



**Fig. 1.** Changes in EF between the first and second examinations in patients with  $EF_1 \leq 40\%$  and  $>40\%$  before release from hospital.

ferences between two observers/mean value of the two observers) was calculated for the ventricular volumes and the EF of the same examinations (evaluated separately by 2 observers).

## RESULTS

### Clinical characteristics

Forty nine of the 74 patients presented with inferolateral infarction, and 25 presented with an anterior infarction (all were assessed by ECG; among the six patients who had no Q wave, SPECT confirmed five inferolateral and one anterior infarction). Fifty three patients were smokers, 34 were hypertensive, and 35 were hypercholesterolemic. Half of the patients presented with pre-infarction angina. Thirteen percent showed a peripheral vasculopathy. Some 40% of the patients received thrombolytic treatment during the first 6 h following the onset of symptoms. None was treated with fibrinolytics after 6 hours. Neither did any receive primary angioplasty. Only 25 patients were catheterized before discharge or during follow-up.

Some 83% of the patients received treatment with beta blockers at the time of the first examination, falling to 61% at the time of the second ( $P<.0001$ ). No significant differences were seen in the number of patients treated with nitrates (15% compared to 22%), calcium antagonists (14% compared to 20%) or inhibitors of angiotensin converting enzyme (16% compared to 19%) at the times of the two examinations.

### Gated SPECT

Interobserver variability was 2.3% ( $r=0.997$ ) for the calculation of diastolic volume, 3.8% ( $r=0.995$ ) for end-systolic volume, and 1.4% ( $r=0.995$ ) for EF.

During the first year after AMI, the EF of the LV improved significantly (from  $46.4 \pm 9.9$  to  $50.9 \pm 11.7\%$ ;  $P<.0001$ ; mean difference 4.5; 95% CI, 0.98-8.00) for the 74 patients as a whole. No significant changes were seen for diastolic volume (from  $104 \pm 34$  to  $105 \pm 39$  ml;  $P=.869$ ; mean difference 0.5; 95% CI, -11.00-12.5), nor for systolic volume (from  $57 \pm 26$  to  $54 \pm 34$  ml;  $P=.278$ ; mean difference 4.5; 95% CI, -7.2 to -12.6), although the latter did show a tendency towards reduction. The increase in EF was significant in the 18 patients with an  $EF=40\%$  (from  $32.2 \pm 5.3$  to  $39.2 \pm 12.5\%$ ;  $P=.035$ ; mean difference 7.0; 95% CI, 0.49-13.5) and in the 56% of patients with an  $EF>40\%$  (from  $50.9 \pm 5.8$  to  $54.6 \pm 8.6\%$ ;  $P=.003$ ; mean difference 3.7; 95% CI, 0.95-6.45) at the time of the first examination (Figure 1).

No significant differences were seen between patients who had received/not received fibrinolytic treatment with respect to ergometric results (MET, maximum cardiac frequency, maximum systolic arterial pressure) or those of gated-SPECT (FE, volumes and indices of perfusion and ischemia). EF increased in the 35 patients who did not receive thrombolytic treatment (from  $46.9 \pm 7$  to  $52.8 \pm 6.2\%$ ;  $P=.006$ ; mean difference 4.5; 95% CI, 1.346-7.654), in the 46 patients treated with beta blockers (from  $45.4 \pm 9$  to  $51.7 \pm 11\%$ ;  $P<.003$ ; mean difference 6.3; 95% CI, 2.14-10.46),

**TABLE 1. Gated SPECT results for inferolateral and anterior infarction patients**

	First examination	Second examination	Mean differences	95% CI	P
<b>Inferolateral (n=49)</b>					
DV, ml	99.4±29.5	96.2±27.7	3.2	-8.3 to 14.7	.260
SV, ml	51.3±19.2	44.3±19.4	7.67	1.5-13.8	.001
EF, (%)	48.±8	54.6±8.7	6.2	2.8-9.5	<.0001
<b>Anterior (n=25)</b>					
DV, ml	114.9±40.1	122.5±52.6	7.6	-18.9 to 34.2	.222
SV, ml)	68.2±33.8	73.9±47	5.7	-17.6 to 28.9	.333
EF, %	42.3±11.9	43.6±13.5	1.3	-5.9 to 8.5	.600

EF indicates ejection fraction; DV, diastolic volume; SV, systolic volume.

and in the 61 patients that did not receive treatment with inhibitors of angiotensin converting enzyme (from 46.9±9 to 51.6±11%; *P*=.011; mean difference 4.7; 95% CI, 1.097-8.3) at the time of the second investigation.

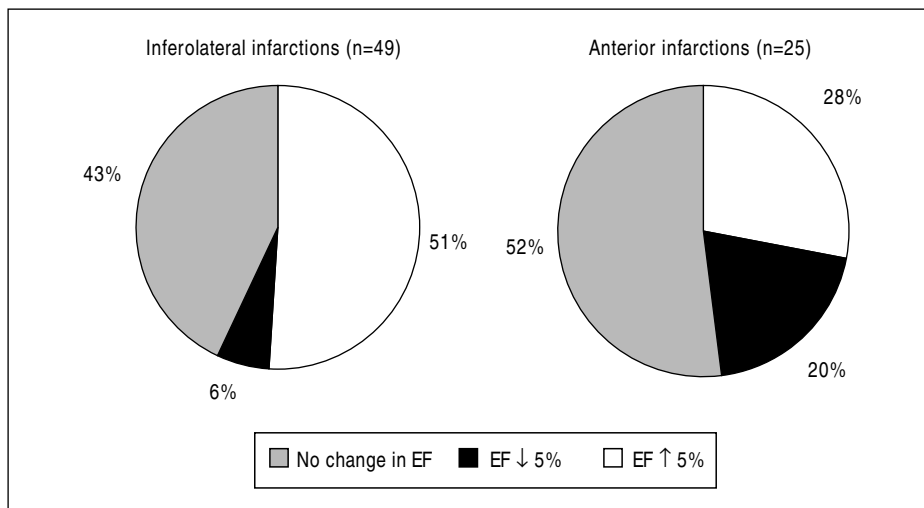
A significant improvement was seen in the systolic volume and EF in patients who had suffered inferolateral infarction, but not in those with an anterior lesion (Table 1). The EF of the LV increased >5% in 25 of the 49 patients (51%) with inferolateral infarction, and in 7 of the 25 (28%) with an anterior infarction (Figure 2).

Significant increases were recorded in maximum O<sub>2</sub> consumption (from 6.2±1 to 7.6±2 MET; *P*<.0001; mean difference 1.4; 95% CI, 0.9-1.9), maximum cardiac frequency (104±19 compared to 125±22 beats/min; *P*<.0001; mean difference 20.4; 95% CI, 13.6-27.1), and maximum systolic pressure (162.2±26 compared to 177.1±29.6 mm Hg; *P*<.0001; mean difference 14.9; 95% CI, 5.8-23.9) between the first and second examinations, although no significant changes were seen in ischemia indices. Nevertheless, there was a significant improvement in the resting perfusion indices in the infarcted region in those who had suffered an inferolateral infarction (Table 2; Figure 3).

## DISCUSSION

In publications reporting the use of isotopic ventriculography between 1 and 10 days post-AMI, the EF of the LV is described to improve in 24%-41% of patients.<sup>7,9,12</sup> In addition, the majority of studies that have compared left ventricular systolic function before hospital discharge with that seen 6 months later, also report significant improvements in EF.<sup>14,15,17,18,20</sup> The fact that other authors<sup>8,11,16</sup> have not found significant differences between EF values in the third and sixth months following AMI seems to support the idea that the majority of these improvements in the first three months following AMI.

The present study used gated SPECT to evaluate the systolic function of the LV and myocardial perfusion before hospital discharge and then again one year after a first AMI. This is a very appropriate technique since evaluations of ventricular volumes and EF are highly reproducible, as reflected in the present results. A little more than half the patients who suffered an inferolateral infarction experienced an increase in EF>5% between the first and second examinations. However, this improvement was seen in only 28% of patients with anterior infarctions; in 20%, the EF



**Fig. 2.** Proportion of patients with changes of >5% in the groups with inferolateral and anterior infarctions.

TABLE 2. Ischemia and perfusion indices at rest in the area of the infarction

	First examination	Second examination	Mean differences	95% CI	P
Inferolateral (n=49)					
Ischemia index	0.22±0.22	0.20±0.19	0.02	-0.06 to 0.10	.505
Perfusion index at rest	2.35±0.25	2.17±0.57	0.18	0.003-0.36	.046
Anterior (n=25)					
Ischemia index	0.20±0.25	0.19±0.26	0.01	-0.13 to 0.15	.919
Perfusion index at rest	2.05±0.75	2.02±0.72	0.03	-0.39 to 0.45	.567

actually fell by >5% (a decrease seen in only 6% of the patients with inferolateral infarction). The increase in EF was significant for patients both with EF=40% or >40% (at the time of the first investigation, and in those who had suffered an inferolateral, but not an anterior infarction. The smaller number of patients with infarctions in the latter area might explain, at least in part, why, unlike in other studies, significance was not reached. Although changes in segmentary contractility between the first and second examinations were not measured, the improvement in global EF in some patients is probably due to improvement in the contractility of the infarcted area since, in all patients, this was normal in all other regions, and none had suffered an infarction at any other site.

The improvement of systolic function has mainly been described in subgroups of patients that have received thrombolytic treatment<sup>26-29</sup> or primary angioplasty,<sup>30</sup> and especially in those with an anterior AMI and low EF. However, in the present study, and in agreement with Warren et al.,<sup>31</sup> EF was also seen to improve in those who had not received thrombolytic treatment. Other authors<sup>32,33</sup> indicate that this improvement could be related to treatment with inhibitors of angiotensin converting enzyme, but in the present study improvements were seen in the EF of patients not treated with these drugs.

An improvement in the systolic function of the LV was also seen in the subgroup of patients on beta blocker treatment one year after AMI.

It has been suggested that the improved perfusion seen in scintigraphs between the acute or subacute phase and the chronic phase in nonrevascularized patients could be due to the spontaneous repermeabilization of the causative artery and/or a recovery of the microcirculation or cell function after the ischemia and reperfusion stage.<sup>34-36</sup> Since only 34% of the present patients were catheterized, the results cannot provide support either way.

Wackers et al.<sup>37</sup> were the first to describe that the proportion of perfusion defects observed with 201Tl diminished over time in patients, following AMI. Pellikka et al.<sup>35</sup> showed that the distribution of perfusion defects diminished between 18-48 h and 6-14 days in patients with re-perfused AMI. Several authors have speculated that this recovery might also be attributed to the development of collateral circulation and the recovery of the microcirculation or transitory alterations to cellular function that contribute to the capture of the radiotracer.<sup>34,37</sup> Toba et al.<sup>38</sup> suggest that the scintigraphic improvement seen in nonsynchronized perfusion images during the follow-up of AMI patients might be due not only to an improvement in perfusion, but also to the recovery of regional contractility in the context of stunned myocardium. The present results appear to support the first of these hypotheses since stunned myocardium corresponds, by definition, to a hypocontractile myocardium with conserved perfusion. The present patients basically showed improvements in the resting perfusion indices of the infarcted

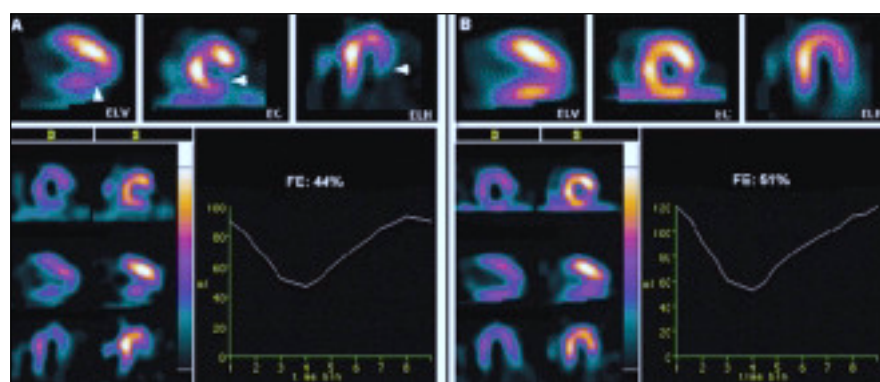


Fig. 3. Gated SPECT of a patient with inferolateral infarction before release from hospital (A) and one year later (B). The upper part of the figure shows the nonsynchronized resting perfusion images of the long vertical axis (ELV), short axis (EC), and long horizontal axis (ELH), showing an important defect of inferolateral perfusion in A (arrows) but a clear improvement in B. The lower part of the figure shows resting perfusion images synchronized in end-diastole (D) and end-systole (S), and the volume curve with ejection fraction (EF) that increased from 45 to 51% between the two examinations.

area between the first and second examinations. In any event, the small number of patients with serious systolic dysfunction allowed no definitive conclusion to be drawn with respect to the possible spontaneous recovery of the viable myocardium.

In conclusion, left ventricular systolic function, as measured by gated SPECT during the first week following an AMI, can change over the following year. In 51% of patients with inferolateral infarction, and in 28% of those with anterior infarction, EF increased by >5% between the first and second examinations. This improvement was accompanied by increased resting myocardial perfusion.

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Candell-Riera J, et al. Evolution of Systolic Function and Myocardial Perfusion, Evaluated by Gated SPECT, in the First Year after Acute Myocardial Infarction

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