Interinstitutional clinical practice guidelines for the treatment of acute myocardial infarction

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Abstract

Introduction: Mexico has the highest 30-day mortality due to acute myocardial infarction (AMI), which constitutes one of the main causes of mortality in the country: 28 % versus 7.5 % on average for the Organization for Economic Co-operation and Development member countries. **Objective:** To establish critical pathways and essential interinstitutional pharmacological strategies for the care of patients with AMI in Mexico, regardless of their socioeconomic status. **Method:** A group of experts in AMI diagnosis and treatment, representatives of the main public health institutions in Mexico, as well as the Mexican cardiology societies, the Mexican Red Cross and representatives of the Spanish Society of Cardiology, were brought together in order to optimize strategies based on the best existing evidence. **Results:** An interinstitutional clinical practice guideline was designed for early diagnosis and timely treatment of AMI with ST-segment elevation, following the clinical horizon of the disease, with the proposal of algorithms that improve the prognosis of patients who attend the emergency services due to an AMI. **Conclusion:** With these clinical practice guidelines, the group of experts proposes to universalize AMI diagnosis and treatment, regardless of patient socioeconomic status.

KEY WORDS: Acute myocardial infarction. Treatment guidelines. Código Infarto.

Guía práctica interinstitucional para el tratamiento del infarto agudo de miocardio

Resumen

Introducción: México tiene la mortalidad más alta a 30 días por infarto agudo de miocardio (IAM), el cual constituye una de las principales causas de mortalidad en el país: 28 % versus 7.5 % del promedio de los países de la Organización para la

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*Cooperación y el Desarrollo Económicos. **Objetivo:** Establecer las rutas críticas y las estrategias farmacológicas esenciales interinstitucionales para la atención de los pacientes con IAM en México, independientemente de su condición socioeconómica. **Método:** Se reunió a un grupo de expertos en diagnóstico y tratamiento de IAM, representantes de las principales instituciones públicas de salud de México, así como las sociedades cardiológicas mexicanas, Cruz Roja Mexicana y representantes de la Sociedad Española de Cardiología con la finalidad de optimizar las estrategias con base en la mejor evidencia existente. **Resultados:** Se diseñó una guía de práctica clínica interinstitucional para el diagnóstico temprano y tratamiento oportuno del IAM con elevación del segmento ST, siguiendo el horizonte clínico de la enfermedad, con la propuesta de algoritmos que mejoren el pronóstico de los pacientes que acuden por IAM a los servicios de urgencias. **Conclusión:** Con la presente guía práctica, el grupo de expertos propone universalizar el diagnóstico y tratamiento en el IAM, independientemente de la condición socioeconómica del paciente.*

PALABRAS CLAVE: Infarto agudo de miocardio. Guía de tratamiento. Código Infarto.

Introduction

In Mexico, 140,000 deaths associated with any cardiac cause were recorded in 2018, mainly due to ischemic heart diseases.¹ In 2017, the Organization for Economic Cooperation and Development classified Mexico as the country with the highest acute myocardial infarction (AMI) mortality rate: 28 % vs. 7.5 %.²

Since 2014, the main public and private health services providers started implementing actions to improve AMI outcomes;³ however, these measures are still far from being universal and patients living in marginalized areas do not receive timely treatment, and establishing regional care systems is therefore necessary.⁴ Such is the case of the Mexican Institute of Social Security *Código Infarto* (Infarction Code) care protocol, which enables efficacious and efficient care to be provided 24 hours a day, 7 days a week (24/7) and all 365 days of the year.⁵

These interinstitutional clinical practice guidelines for early diagnosis and timely treatment of ST-segment elevation acute myocardial infarction (STEMI) were developed with the purpose to establish critical pathways and essential inter-sectoral pharmacological strategies for the universal care of patients with AMI in Mexico.

Methods

A group of experts in the diagnosis and treatment of STEMI was created, which included representatives of the main public health institutions of Mexico, Mexican cardiology societies, the Mexican Red Cross and the Spanish Society of Cardiology, with the purpose to optimize strategies based on the best existing evidence according to current clinical practice guidelines. Actions were proposed based on evidence or general agreement

that the treatment or procedure is beneficial, useful and effective, deriving from multiple clinical trials, meta-analyses or large non-randomized clinical studies; in case of controversy, an agreement was reached by the expert group.⁶ The approach was to infarction natural history, timely diagnosis and reperfusion treatment; face-to-face and online panel discussions were held, until interinstitutional consensus was arrived at.

Diagnostic criteria

To define ST-segment elevation, two initial criteria are required: clinical and electrocardiographic criteria; as well as two complementary criteria: cardiac biomarkers elevation and mobility alterations demonstrated by some imaging method (Fig. 1).

Clinical criterion

Crushing or oppressive chest pain, which can be accompanied by dyspnea and neurovegetative symptoms, of sudden onset and progressive, lasting more than 20 minutes, radiating to the left shoulder and arm, neck and left branch of the jaw. It can be absent in patients with diabetes, old age and in women.

Electrocardiographic criterion

ST-segment elevation that appears in two contiguous leads minutes after symptoms' onset (Table 1). With a 12- to 16-lead electrocardiogram in less than 10 minutes of medical contact, reperfusion strategy is decided (Fig. 2).

Biochemical criterion

Cardiac troponin T7 or I elevation above the 99th percentile of normal level, preferably high-sensitivity, in addition to the above criteria (Table 2).

Figure 1. Diagnostic algorithm for STEMI at emergency departments. DL = dyslipidemia, DM = diabetes mellitus, SAH: systemic arterial hypertension, STEMI: ST-segment elevation acute myocardial infarction, NSTEMI-ACS: Non-ST-segment elevation acute coronary syndrome.

Table 1. Current electrocardiographic criteria that confirm ST-segment elevation acute myocardial infarction diagnosis

1. New ST-segment elevation in two contiguous leads:
 - ≥ 0.1 mV in DI, DII, DIII, AVL, AVF, V4-V6; as well as in optional V7, V8 left and V9 and right leads (V3 and V4).
 - In precordial leads: ≥ 0.15 mV in V1 to V3 in women; ≥ 0.2 mV, in V1 to V3 in men > 40 years; ≥ 0.25 mV in V1 to V3 in men < 40 years.
2. New-onset left bundle block.
3. New-onset right bundle branch block, which, in addition, is considered of poor prognosis.
4. New-onset Q wave in two contiguous leads.

*The electrocardiogram should be interpreted by an expert or be submitted via telemetry, HL7 (Health Level Seven International) or GPS to an expert center.

Figure 2. Electrocardiogram showing ST-segment elevation in the lower and anterolateral region, where the diagnostic criterion for ST-segment elevation acute myocardial infarction is met.

Imaging criterion

At emergency department, echocardiogram allows mobility disorders (hypokinesia or akinesia) and thickness of the affected area to be identified.

Treatment

Reperfusion treatment is the cornerstone in STEMI and should be carried out as soon as possible. Time-liness translates into a recovered myocardium and lower mortality; in addition, adjunctive therapy is essential.

Reperfusion therapy in STEMI

It should be implemented in all patients in less than 12 hours of evolution with primary percutaneous coronary intervention (pPCI) or fibrinolytic therapy (FT); both are equivalent during the first two hours of

Table 2. Determination of cardiac biomarkers that confirm ST-segment elevation acute myocardial infarction diagnosis

Protein	First detection	Duration	Sensitivity	Specificity
Myoglobin	1.5-2 hours	8-12 hours	+++	+
CPK-MB	2-3 hours	1-2 days	+++	+++
Troponin I*	3-4 hours	7-10 days	++++	++++
Troponin T*	3-4 hours	7-14 days	++++	++++
CPK	4-6 hours	2-3 days	++	++

CPK = Creatine phosphokinase, MB = MB fraction.

*High-sensitivity.

Table 3. Different pharmacological treatment regimens for specific fibrinolytic therapy

Drug	Treatment regimen
Alteplase (rt-PA)	100 mg in 60 minutes: 20-mg bolus, followed by 80-mg infusion over 60 minutes; INC dose for patients > 67 kg. Alteplase accelerated dosing is recommended in patients weighing less than 67 kg. 15-mg IV bolus, followed by 0.75 mg/kg (max 50 mg) over 30 min, then 0.5 mg/kg (up to 35 mg) over 60 min.
Tenecteplase (TNK)	5- or 10-second bolus, calculated based on weight: – < 60 kg: 30 mg-6 mL – 61 to 70 kg: 35 mg-7 mL – 71 to 80 kg: 40 mg-8 mL – 81 to 90 kg: 45 mg-9 mL – > 91 kg: 50 mg-10 mL

symptoms onset, although pPCI is preferred if a hemodynamics unit is available, and FT when a hemodynamics unit is not available or if the time to pPCI is longer than 120 minutes (Fig. 3). Mortality can be similar with FT and pPCI within the first 114 minutes;⁸ thus, FT should be implemented in less than 30 minutes (ideally in less than 10 minutes).

Prehospital fibrinolytic therapy

Benefit has been shown in some countries, with higher 1-year survival.⁹ It is recommended within the first three hours of first medical contact and when transfer time is longer than 120 minutes. Fibrinolytic-specific agents at correct doses are preferred (Tables 3 and 4), and it is essential for high-tech ambulances to be available, equipped with defibrillator monitors, full equipment for cardiopulmonary resuscitation and intravenous anti-arrhythmic drugs.

STEMI care networks

Two types of STEMI care networks will be integrated: one with reference to hospitals with a hemodynamics

unit where there should be adequate communication and coordination in order to prioritize pPCI in less than 120 minutes after diagnosis (Fig. 4A), and one with reference to hospitals that lack a hemodynamics unit, which will be the majority in Mexico, and where FT performance should be prioritized as soon as possible in no more than 30 minutes (ideally no more than 10 minutes) (Fig. 4B).

Fibrinolytic therapy

It should be implemented within the first 120 minutes after diagnosis with fibrinolytic-specific agents (Tables 3 and 4), as long as there are no contraindications.¹⁰ The benefit is attributed to this treatment and to antiplatelet agents.

Pharmacoinvasive strategy

It is the interventional procedure after FT that is appropriate within the first two to 24 hours; the results are comparable to those of pPCI.¹¹⁻¹³ The time of equivalence between pharmacoinvasive strategy and pPCI is approximately 100 minutes. In patients

Figure 3. Universal reperfusion algorithm for patients with ST-segment elevation acute myocardial infarction. TIT = total ischemic time, FMC = first medical contact, ECG = Electrocardiogram, STEMI = ST-segment elevation acute myocardial infarction, GC = intracoronary guidewire crossing, FMC-GC = first medical contact-intracoronary guidewire crossing, FT = fibrinolytic therapy, pPCI = primary percutaneous coronary intervention, rPCI = rescue percutaneous coronary intervention, ePCI = elective percutaneous coronary intervention, Pre-H = pre-hospital.

with failed fibrinolysis, rescue percutaneous coronary intervention should be immediately implemented.¹³

Primary percutaneous coronary intervention (pPCI)

Coronary flow restoration is the primary therapeutic objective in the care of patients with STEMI, and is associated with a lower occurrence of early death, re-infarction, cardiogenic shock and hemorrhagic complications.¹³ It requires sufficient infrastructure and adequately trained personnel (Fig. 3). For its

performance, the following aspects should be considered:¹³

- Radial approach as first choice.
- Adequate anticoagulation and platelet inhibition.
- Contrast medium use minimization.
- Excessive coronary manipulation avoidance.
- Drug-eluting stents implantation.

Considerations for PCI in the COVID-19 era

Hemodynamics units' activities in the context of the COVID-19 epidemic¹⁴ have two main objectives: on

Table 4. Fibrinolytic therapy indications and contraindications

Indications	Absolute contraindications
<p>Chest pain suggestive of ischemia > 20 minutes associated with: ST-segment persistent elevation</p> <ul style="list-style-type: none"> - > 0.01 mV in two or more contiguous bipolar leads. - > 0.02 mV in two contiguous precordial leads. <p>De novo left bundle branch block, - ST-segment depression from V1 to V3, with early transition and ST-segment elevation in posterior leads (V7 to V9). Up to 12 hours from symptoms onset. No absolute contraindication.</p>	<ul style="list-style-type: none"> - Systolic blood pressure > 180 to 200 mmHg. - Diastolic blood pressure > 100 to 110 mmHg. - Difference between right and left arm systolic pressure > 15 mmHg. - History of central nervous system structural disease. - Closed head or face trauma within previous 3 months. - Major trauma (2 to 4 weeks), surgery (ophthalmologic laser) or gastrointestinal bleeding. - Active bleeding or hematological problems. - History of intracranial hemorrhage. - Ischemic stroke within > 3 hours and < 3 months. - Pregnancy. - Serious systemic disease (end-stage cancer, end-stage kidney or liver disease).

Figure 4. ST-segment elevation acute myocardial infarction care networks in hospitals with hemodynamics unit with the possibility of pPCI (A) and with no hemodynamics unit but with the possibility of fibrinolytic therapy at the site of diagnosis (B). The indication is to proceed with pharmacoinvasive strategy at between 2 and 24 hours of fibrinolytic therapy in hospitals with hemodynamics unit.

one hand, resource optimization (personnel, beds, means of transport), and on the other, prevention of transmission to patients and professionals with the use of personal protective equipment.

pPCI continues to be the choice in patients with less than 12 hours of symptoms onset, or for those in whom symptoms persist or are unstable; FT is considered of choice in centers without a hemodynamics unit (Fig. 4B) when time to reperfusion exceeds 120 minutes. In patients with multivessel disease,¹⁵ outside the context of cardiogenic shock, complete revascularization is recommended in the same procedure or

in a deferred manner, always trying to favor early hospital discharge.

Coronary angiography is not recommended in patients who underwent cardiorespiratory resuscitation when electrocardiographic diagnosis is not infarction.¹⁶ In cardiogenic shock, early intubation prior to the procedure (closed circuits) and prioritizing extracorporeal membrane oxygenation assistance is recommended. Interactions of the most commonly used drugs in cardiology with possible treatments for COVID-19 should be considered.

Table 5. Adjuvant drugs for the treatment of ST-segment elevation acute myocardial infarction

Drug	Action	Dose	Contraindications/precautions	Duration
Antiplatelet agents				
Acetylsalicylic acid	It irreversibly inactivates the cyclooxygenase enzyme, thus suppressing the production of thromboxane A ₂ , an essential element for platelet activation and aggregation.	Fibrinolysis and pPCI Loading: 150-300 mg PO. Maintenance: 75-150 mg/day PO.	– Acetylsalicylic acid allergy. – Recent or active gastrointestinal bleeding.	Indefinitely (for life).
Clopidogrel	Thienopyridine, platelet ADP inhibitor (P2Y ₁₂ subunit). This drug is added to acetyl salicylic acid treatment for so-called double antiplatelet therapy (DAPT).	Fibrinolysis Loading: 300 mg PO. Maintenance: 75 mg/day PO. > 75 years: loading dose is eliminated and only the maintenance dose is administered. pPCI Loading: 600 mg PO. Maintenance: 75 mg/day PO.	– Active hemorrhage.	At least 12 months.
Prasugrel	Thienopyridine, platelet ADP inhibitor (P2Y ₁₂ subunit). It is added to acetylsalicylic acid treatment for DAPT.	pCPI Loading: 60 mg PO. Maintenance: 10 mg/day PO.	– Indicated only when coronary anatomy is known. – Contraindicated in patients with a history of stroke, severe liver failure and age ≥ 75 years. – Patients weighing ≤ 60 kg: administer maintenance doses of 5 mg/day PO.	12 months
Ticagrelor	Cyclopentyl-triazolopyrimidine, platelet ADP inhibitor (P2Y ₁₂ subunit). It is added to acetylsalicylic acid treatment for DAPT.	pPCI Loading: 180 mg PO. Maintenance: 90 mg every 12 hours PO.	– Active hemorrhage. – Relevant side effects: dyspnea and bradycardia.	12 months
Glycoprotein IIb/IIIa inhibitors: – Abciximab – Tirofiban – Eptifibatide	These drugs inhibit fibrinogen binding to platelet glycoprotein IIb/IIIa receptor by interrupting the process of platelet aggregation.	– pPCI (only used in hemodynamics laboratory) – Abciximab: 0.25 mg/kg IV bolus and 0.125 µg/kg/minute infusion. – Tirofiban: 25 µg/kg IV over 3 minutes followed by 0.15 µg/kg/minute maintenance infusion. – Eptifibatide: 180-µg/kg double IV bolus (administered at 10-minute intervals), followed by 2 µg/kg/minute infusion.	– Active hemorrhage. – Thrombocytopenia.	– Abciximab: 12 hours. – Tirofiban: 18 hours. – Eptifibatide: 18 hours.

(Continues)

Table 5. Adjuvant drugs for the treatment of ST-segment elevation acute myocardial infarction (Continued)

Drug	Action	Dose	Contraindications/precautions	Duration
Anticoagulants				
Unfractionated heparin	Stimulates anti-thrombin III activity, which inhibits coagulation cascade factors Xa and IIa.	Fibrinolysis 60 IU/kg IV bolus, up to 4,000 IU, followed by 12 IU/kg IV infusion, up to 1000 IU/h over 24 to 48 h. aPTT target 50-70 seconds or 1.5 to 2 times the control value. pPCI 70-100 IU/kg IV bolus when administration of a glycoprotein IIb/IIIa inhibitor is not planned. 50 to 70 IU/kg IV bolus with glycoprotein IIb/IIIa inhibitors.	– Active hemorrhage. – Thrombocytopenia.	24 to 48 hours.
Low-molecular-weight heparin (enoxaparin)	Inhibits coagulation cascade factors Xa and IIa.	Fibrinolysis For < 75 years of age: 30 mg IV bolus followed, at 15 min, by 1 mg/kg SC every 12 hours. First two doses: not to exceed 100 mg each. For > 75 years of age: IV bolus is not administered; start with a dose of 0.75 mg/kg SC every 12 hours (up to 75 mg per injection for the first two doses). Creatinine clearance < 30 mL/minute: SC dose every 24 hours. pPCI 0.5 mg/kg IV bolus.	– Active hemorrhage.	Until coronary artery bypass grafting or hospital discharge (for up to 8 days).
Co-adjuvant therapy				
Nitroglycerin	Coronary vasodilator that attenuates myocardial ischemia-derived symptoms by reducing afterload and increasing coronary blood flow. It is used to control angina (either orally or intravenously). In ST-segment elevation acute myocardial infarction, the highest benefit is observed in uncontrolled systemic arterial hypertension or acute heart failure (intravenously administered).	One 0.3 or 0.4 mg sublingual tablet, up to a total of 3 doses at 5-minute intervals. Intravenously, it is started at 10 to 20 µg/min and is adjusted according to the therapeutic response (increasing from 5 to 10 µg/min every 5 to 10 minutes until the desired effect is obtained).	– Hypotension. – Unstable tachycardia or bradycardia – Myocardial infarction with right ventricle extension. – Use of phosphodiesterase inhibitors for erectile dysfunction (or for pulmonary arterial hypertension) within the last 24 to 48 hours.	Infusion over 48 hours.
Beta-adrenergic blockers – Metoprolol – Bisoprolol – Carvedilol	These agents inhibit circulating catecholamines activity and decrease myocardial oxygen consumption. They reduce heart ischemia, re-infarction and tachyarrhythmias. Have been shown to decrease mortality.	– Metoprolol succinate: 12.5-100 mg every 24 hours. – Bisoprolol: 1.25-10 mg every 24 hours. – Carvedilol: 3.125-25 mg every 12 hours.	– Heart failure. – Hypotension (systolic blood pressure ≤ 100 mmHg). – Bradyarrhythmias. – Asthma.	For life. Adjust for hemodynamic status, acute or chronic pathology or side effects.

(Continues)

Table 5. Adjuvant drugs for the treatment of ST-segment elevation acute myocardial infarction (Continued)

Drug	Action	Dose	Contraindications/precautions	Duration
Angiotensin-converting enzyme inhibitors – Captopril – Enalapril – Ramipril – Perindopril	These drugs inhibit the renin-angiotensin-aldosterone system and limit the cardiac remodeling phenomenon (dilatation). Especially useful in patients with heart failure, diabetes mellitus or anterior myocardial infarction.	– Captopril: 6.25-50 mg every 8 hours. – Enalapril: 2.5-20 mg every 12 hours. – Ramipril: 2.5-10 mg every 24 hours. – Perindopril 2-4 mg every 24 hours	– Hypotension. – Cardiogenic shock. – Kidney failure. – Hyperkalemia. – Intolerance to the drug.	For life. Adjust for hemodynamic status, acute or chronic pathology or side effects.
Angiotensin II type 1 receptor blockers – Valsartan – Candesartan – Olmesartan – Telmisartan – Irbesartan	These drugs inhibit the renin-angiotensin-aldosterone system and limit the cardiac remodeling phenomenon (dilatation). Especially useful in patients with heart failure, diabetes mellitus or anterior myocardial infarction.	– Valsartan: 40-160 mg every 12 hours. – Candesartan: 4-32 mg every 24 hours. – Olmesartan: 20-40 mg every 24 hours. – Telmisartan: 40-80 mg every 24 hours – Irbesartan: 150-300 mg every 24 hours	– Hypotension. – Cardiogenic shock. – Kidney failure. – Hyperkalemia. – Intolerance to the drug.	For life. Adjust for hemodynamic status, acute or chronic pathology or side effects.
Mineralocorticoid receptor antagonists – Spironolactone – Eplerenone	These drugs antagonize aldosterone action. Indicated when there is LVEF $\leq$ 40 % or data consistent with heart failure or diabetes mellitus. Require prior management with angiotensin-converting enzyme inhibitors (or angiotensin II receptor blockers) and beta-blockers.	– Spironolactone: 25-50 mg every 24 hours. – Eplerenone: 25-50 mg every 24 hours.	– Hypotension. – Cardiogenic shock. – Kidney failure. – Hyperkalemia. – Intolerance to the drug.	For life. Adjust for hemodynamic status, acute or chronic pathology or side effects.
3-hydroxy-3-methyl glutaryl-coenzyme A reductase inhibitors (statins) – Simvastatin – Rosuvastatin – Atorvastatin	Lipid-lowering agents that modulate and attenuate inflammatory response and improve endothelial function. These effects are called pleiotropic.	– Atorvastatin: 80 mg/day. – Simvastatin: 40 mg/day. – Rosuvastatin: 40 mg/day.	– Myopathy. – Rhabdomyolysis. – Liver failure.	For life. Adjust for hemodynamic status, acute or chronic pathology or side effects.

Adjuvant treatment

For STEMI comprehensive treatment, the patient should receive general measures since admission to the emergency department, including oxygen if saturation is $\leq 90\%$, analgesia (5 mg of morphine as initial dose and 2.5 to 5 mg every 10 to 15 minutes), and intravenous drips should be started with solution and adjuvant therapy (Table 5).

Risk stratification by scales in STEMI

It is used to predict in-hospital mortality, to identify patients at high risk of death, and low-risk subjects who do not require invasive procedures, as well as to plan cardiac rehabilitation and secondary prevention after the acute episode. The most widely used scales are GRACE¹⁷ and the Thrombolysis in Myocardial Infarction (TIMI)¹⁸ scale, which early identify risk by dividing patients into low-, intermediate- or high-risk.

Early cardiac rehabilitation

It is recommended from the first 24 to 48 hours in the intensive care unit and hospitalization, to be continued at discharge and patient reintegration to his/her family, social and work spheres. Rehabilitation programs include three phases, as reported by Justiniano et al.:¹⁹ the first one corresponds to the hospitalization period (mobilization and stretching); the second one is the period after discharge (prescription of exercise, risk factors modification, education with regard to the disease and reintegration to work-related activities); and the third one, inclusion in self-help groups. Early cardiac rehabilitation allows early discharge from intensive care and hospitalization, better quality of life and fewer days of disability leave.

Discussion

In Mexico, the health system is fractionated and some strategies are not homogeneously applied in the country; therefore, these interinstitutional clinical practice guidelines represent the first approach to universalize STEMI diagnosis and treatment, considering the right to health recovery. The heavy burden of disease in the Mexican population, resulting from the high prevalence of risk factors, should motivate primary prevention programs, timely care of cardiovascular emergencies, secondary prevention and rehabilitation.²⁰

FT and the pharmacoinvasive strategy can be an alternative in Mexico, with the possibility for time to reperfusion to be optimized in the care process.^{21,22} Health care systems should ideally seek STEMI universal reperfusion, which is why the importance of the recommendations of the first interinstitutional guidelines in Mexico stands out. In COVID-19 patients, FT is recommended if symptoms do not exceed three hours of evolution and the patient is stable; in our country, it can be a strategy that benefits patients with a poor clinical situation.

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