

Título completo:	Mechanical complications in STEMI: Prevalence and mortality trends in the primary PCI era. Ruti-STEMI Registry
Resumen:	ABSTRACT Introduction and objectives: Mechanical complications confer a dreadful prognosis in ST elevation myocardial infarction (STEMI). Their prevalence and prognosis are unsettled in the current era of primary percutaneous coronary intervention (PPCI) reperfusion networks. We aimed to analyze prevalence and mortality trends of post-STEMI mechanical complications during 2 decades, before and after PPCI networks were established. Methods: Prospective, consecutive registry of STEMI patients within a region of 850 000 inhabitants during 2 decades: a pre-PPCI period (1990-2000) and a PPCI period (2007-2017). We analyzed the prevalence of mechanical complications, including ventricular septal rupture, papillary muscle rupture, and free wall rupture (FWR). Twenty-eight-day and 1-year mortality trends were compared between the 2 studied decades. Results: A total of 6033 STEMI patients were included (pre-PPCI period, n = 2250; PPCI period, n = 3783). Reperfusion was supported by thrombolysis in the pre-PPCI period (99.1%), and by PPCI in the PPCI period (95.7%). Mechanical complications developed in 135 patients (2.2%): 38 ventricular septal rupture, 24 papillary muscle rupture, and 73 FWR patients. FWR showed a relative reduction of 60% in the PPCI period (0.8% vs 2.0%, $P < .001$), without significant inter-period changes in the other mechanical complications. After multivariate adjustment, FWR remains higher in the pre-PPCI period (OR, 1.93; 95%CI, 1.10-3.41; $P = .023$). At 28-day and 1-year, mortality did not show significant changes in all studied mechanical complications. Conclusions: The establishment of regional PPCI networks has modified the landscape of mechanical complications in STEMI. FWR is less frequent in the PPCI era, likely due to reduced transmural infarcts. RESUMEN Introducción y objetivos: Las complicaciones mecánicas (CM) confieren un mal pronóstico en el infarto de miocardio con elevación del ST (IAMCEST). Su prevalencia y pronóstico son inciertos en la era de la angioplastia primaria (AP). Analizamos las tendencias de prevalencia y mortalidad de las CM post-IAMCEST durante 2 décadas, antes y después de que se establecieran las redes de AP. Métodos: Registro prospectivo y consecutivo de pacientes con IAMCEST en una región de 850.000 habitantes durante 2 décadas: periodo pre-AP (1990-2000) y periodo AP (2007-2017). Analizamos la prevalencia de CM (comunicación interventricular, ruptura del músculo papilar y ruptura de pared libre [RPL]). Se compararon las tendencias de mortalidad a 28 días y 1 año. Resultados: Se incluyó a 6.033 pacientes con IAMCEST (pre-AP, n = 2.250; AP, n = 3.783). La reperusión fue apoyada por trombólisis en el periodo pre-AP (99,1%) y por AP en el periodo AP (95,7%). Hubo CM en 135 pacientes (2,2%): 38 comunicación interventricular; 24 ruptura del músculo papilar y 73 RPL. La RPL mostró una reducción relativa del 60% en el periodo de AP (0,8% frente a 2,0%, $p < 0,001$), sin cambios significativos en las demás CM. Después del ajuste multivariable, la RPL sigue siendo mayor en el periodo pre-AP (OR = 1,93; IC95%, 1,10-3,41; $p = 0,023$). La mortalidad no mostró cambios significativos en ninguna de las CM. Conclusiones: El establecimiento de redes regionales de AP ha modificado el panorama de las CM en el IAMCEST. La RPL es menos frecuente en la era de la AP, probablemente debido a la reducción de los infartos transmurales.
Palabras clave:	STEMI, mechanical complications, free wall rupture, ventricular septal rupture, papillary muscle rupture, primary percutaneous coronary intervention.
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Mechanical complications in STEMI: Prevalence and mortality trends in the primary PCI era.

Ruti-STEMI Registry

Complicaciones mecánicas en IAMEST: Tendencias de prevalencia y mortalidad en la era de la angioplastia primaria. Registro Ruti-STEMI

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ABSTRACT

Introduction and objectives: Mechanical complications confer a dreadful prognosis in ST elevation myocardial infarction (STEMI). Their prevalence and prognosis are unsettled in the current era of primary percutaneous coronary intervention (PPCI) reperfusion networks. We aimed to analyze prevalence and mortality trends of post-STEMI mechanical complications during 2 decades, before and after PPCI networks were established.

Methods: Prospective, consecutive registry of STEMI patients within a region of 850 000 inhabitants during 2 decades: a pre-PPCI period (1990-2000) and a PPCI period (2007-2017). We analyzed the prevalence of mechanical complications, including ventricular septal rupture, papillary muscle rupture, and free wall rupture (FWR). Twenty-eight-day and 1-year mortality trends were compared between the 2 studied decades.

Results: A total of 6033 STEMI patients were included (pre-PPCI period, $n = 2250$; PPCI period, $n = 3783$). Reperfusion was supported by thrombolysis in the pre-PPCI period (99.1%), and by PPCI in the PPCI period (95.7%). Mechanical complications developed in 135 patients (2.2%): 38 ventricular septal rupture, 24 papillary muscle rupture, and 73 FWR patients. FWR showed a relative reduction of 60% in the PPCI period (0.8% vs 2.0%, $P < .001$), without significant inter-period changes in the other mechanical complications. After multivariate adjustment, FWR remains higher in the pre-PPCI period (OR, 1.93; 95%CI, 1.10-3.41; $P = .023$). At 28-day and 1-year, mortality did not show significant changes in all studied mechanical complications.

Conclusions: The establishment of regional PPCI networks has modified the landscape of mechanical complications in STEMI. FWR is less frequent in the PPCI era, likely due to reduced transmural infarcts.

Keywords: STEMI . Mechanical complications . Free wall rupture . Heart rupture . Ventricular septal rupture . Papillary muscle rupture . Primary percutaneous coronary intervention.

RESUMEN

Introducción y objetivos: Las complicaciones mecánicas (CM) confieren un mal pronóstico en el infarto de miocardio con elevación del ST (IAMCEST). Su prevalencia y pronóstico son inciertos en la era de la angioplastia primaria (AP). Analizamos las tendencias de prevalencia y mortalidad de las CM post-IAMCEST durante 2 décadas, antes y después de que se establecieran las redes de AP.

Métodos: Registro prospectivo y consecutivo de pacientes con IAMCEST en una región de 850.000 habitantes durante 2 décadas: periodo pre-AP (1990-2000) y periodo AP (2007-2017). Analizamos la prevalencia de CM (comunicación interventricular, ruptura del músculo papilar y ruptura de pared libre [RPL]). Se compararon las tendencias de mortalidad a 28 días y 1 año.

Resultados: Se incluyó a 6.033 pacientes con IAMCEST (pre-AP, n = 2.250; AP, n = 3.783). La reperusión fue apoyada por trombólisis en el periodo pre-AP (99,1%) y por AP en el periodo AP (95,7%). Hubo CM en 135 pacientes (2,2%): 38 comunicación interventricular; 24 ruptura del músculo papilar y 73 RPL. La RPL mostró una reducción relativa del 60% en el periodo de AP (0,8% frente a 2,0%, $p < 0,001$), sin cambios significativos en las demás CM. Después del ajuste multivariable, la RPL sigue siendo mayor en el periodo pre-AP (OR = 1,93; IC95%, 1,10-3,41; $p = 0,023$). La mortalidad no mostró cambios significativos en ninguna de las CM.

Conclusiones: El establecimiento de redes regionales de AP ha modificado el panorama de las CM en el IAMCEST. La RPL es menos frecuente en la era de la AP, probablemente debido a la reducción de los infartos transmurales.

Palabras clave: IAMCEST. Complicaciones mecánicas. Ruptura de la pared libre. Ruptura cardiaca. Rotura del tabique ventricular. Comunicación interventricular. Ruptura del músculo papilar. Angioplastia primaria. Intervención coronaria percutánea primaria.

Abbreviations

FWR: free wall rupture

MC: mechanical complications

PMR: papillary muscle rupture

PPCI: primary percutaneous coronary intervention

STEMI: ST elevation myocardial infarction

VSR: ventricular septal rupture

Abreviaturas

AP: angioplastia primaria

CIV: ruptura del tabique ventricular

CM: complicaciones mecánicas

IAMCEST: infarto de miocardio con elevación del segmento ST

RMP: ruptura del músculo papilar

RPL: rotura de pared libre

INTRODUCTION

Worldwide, ischemic heart disease is the single most common cause of death.^{1,2} Recent studies have shown a decrease in acute and long-term mortality after ST elevation myocardial infarction (STEMI), mostly driven by the widespread use of reperfusion therapies, mainly primary percutaneous coronary intervention (PPCI), modern antithrombotic therapy, and secondary prevention.^{3,4} The main cause of in-hospital mortality after STEMI is cardiogenic shock, which is responsible for > 50% of early deaths, followed by mechanical complications (MC), which account for approximately one-third of early deaths.⁵⁻⁸

MC include rupture of the left ventricular free wall (FWR), rupture of the interventricular septum (VSR), and papillary muscle rupture (PMR).⁹⁻¹¹ Classically, reported risk factors for MC development were female sex, advanced age, hypertension, higher heart rate, delayed admission, or late thrombolysis.¹² FWR of the infarcted ventricle is relatively common in patients with acute post-infarct death. Several large studies have found cardiac rupture in 14-26% of such patients.^{13,14} Data reported in the late 20th

century indicates that thrombolysis reduced the incidence of FWR compared to no reperfusion.¹⁵⁻¹⁷ Relative to VSR, its incidence was found to be low (around 0.2%) in patients receiving thrombolysis in GUSTO-I trial,¹⁵ although an increased risk of septal rupture was observed in patients with single-vessel disease (especially of the left anterior descending artery), extensive myocardial damage, and poor septal collateral circulation.^{16,17} The CIVIAM, a recent Spanish registry including VSR showed a reduction in one-year mortality in the last years, although the relation with the type of reperfusion therapy or specific changes in the incidence were not completely reported.¹⁸ Finally, PMR is a life-threatening STEMI complication that accounts for approximately 5% of deaths in these patients.¹¹ Most of the data available on MC incidence and outcomes are from classical studies using thrombolysis. The impact of PPCI on MC within STEMI networks is unsettled. Accordingly, we aimed to analyze changes in incidence and mortality trends (at 28 days and 12 months) of post-STEMI MC during 2 decades: a decade before and a decade after the set-up of PPCI networks.

METHODS

Study population

This is an analysis from the Ruti-STEMI registry⁴, a prospective population-based registry of a single tertiary hospital, maintained from February 1989 through December 2017. Our hospital is the hub center of 4 second-level hospitals, and including all consecutive STEMI patients serving a stable and well-defined geographical area of ~850 000 inhabitants.

Until the year 2000, reperfusion therapy was mainly performed with thrombolysis. Since 2007, PPCI has been prioritized for all STEMI patients at all hours every day of the week, a program that later crystallized in the Catalonia Codi IAM STEMI network. For the purpose of this study, we compared 2 decades, one representative of the thrombolysis era, the pre-PPCI period (1990-2000), and the other with PPCI management or PPCI period (2007-2017). Between 2000 and 2007, thrombolysis and PPCI

coexisted (the latter only during working hours), and this period was excluded from the present analysis.

Post-STEMI MC trends in prevalence, management, and mortality (at 28 days and 12 months) were analyzed. Mortality was curated from patient health records and/or by direct phone contact with patients or relatives and double-verified by the Catalan and Spanish health system databases.

All study procedures were in accordance with the ethical standards outlined in the Declaration of Helsinki. Patients provided written consent for use of their clinical data for research purposes.

Definitions

STEMI definition was based on current guidelines available during the study life span.¹⁹⁻²¹ STEMI was defined as ST elevation of ≥ 1 mm in at least 2 contiguous leads (in V2-V3 ≥ 2 mm was required) in any location in the index or qualifying electrocardiogram.

MC was defined as any spontaneous rupture of the myocardium following STEMI. It comprises 3 types, according to the area where the myocardial rupture happens: FWR, VSR, and PMR. Confirmed FWR was defined as the occurrence of electromechanical dissociation or severe and sudden hemodynamic compromise associated with at least one of the following: *a*) pericardial effusion (> 1 cm) with intrapericardial echoes and criteria of cardiac tamponade by 2-dimensional echocardiography; *b*) hemopericardium by pericardiocentesis; or *c*) anatomic confirmation (surgical or post-mortem). VSR was diagnosed by Doppler echocardiography, ventriculography, surgical closure of the ruptured site, or necropsy. PMR was diagnosed by transthoracic or transesophageal Doppler echocardiography or by anatomic confirmation (surgery or necropsy). Patients with functional mitral regurgitation secondary to acute papillary muscle dysfunction but without evidence of rupture were not included.

Statistical analysis

Categorical variables were expressed using frequency and percentages. Continuous variables were expressed as the mean (standard deviation, SD). Statistical differences between groups were

1 compared using the chi-squared or Student *t* test. Departures from normality were evaluated using
2 normal Q-Q plots. Multivariate analysis was performed with logistic regression, modeling with the
3 following covariates: age, sex, hypertension, previous infarction, infarct location and reperfusion.
4 Assumption of linearity of continuous variables (logistic regression) was tested. Probability values < .05
5 from 2-sided tests were considered to indicate statistical significance. All analyses were performed
6 using the software IBM Statistics SPSS 21 (IBM Corp., United States).
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16 RESULTS

17 A total of 6033 consecutive STEMI patients were included in this analysis. The mean age was 61.7 years
18 (SD, 12.8) and 78.8% were men. The pre-PPCI period (1990-2000) included 2250 patients, and the PPCI
19 (2007-2017), 3783 patients. Baseline demographic and clinical characteristics are shown in table 1.
20 Patients in the PPCI period were older (62.4 vs 60.4 years, $P < .001$) and more often had hypertension
21 and dyslipidemia, with lower rates of peripheral disease or previous myocardial infarction than those
22 of the pre-PPCI period. Diagnosis criteria of hypertension, diabetes or dyslipidemia have been changed
23 during the years of the registry. This fact could influence in these differences between periods. Patients
24 with Killip-Kimball class III-IV declined from the pre- to the PPCI period by 35% (14.7% vs 9.5%). In the
25 PPCI period, more than 80% of patients evolved without any sign of heart failure (Killip-Kimball class
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42 Table 1 shows medical management of the studied patients in the 2 periods. In the PPCI period a
43 significant increase in the use of antiplatelet drugs, beta-blockers, statins, and rennin-angiotensin-
44 aldosterone system inhibitors was observed. Nevertheless, key differences were found between the 2
45 studied periods relative to the reperfusion strategy. First, reperfusion increased by ~1.8 fold between
46 the pre- and PPCI periods. Second, among reperfused patients, 99.1% received thrombolysis in the
47 pre-PPCI period, whereas 95.7% received PPCI in the PPCI period.
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57 MC developed in 135 patients (2.2%), including 73 patients (1.2%) with FWR, 38 (0.6%) with VSR, and
58 24 (0.4%) with PMR (table 2). The prevalence of MC as a whole declined by 41% from the pre- to the
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PPCI period (from 3.0% to 1.8%, respectively, $P < .001$), mainly due to reduction in FWR. FWR experienced a relative reduction of 60% in the PPCI period (2.0% vs 0.8%, $P < .001$), without significant inter-period changes for VSR (0.7% vs 0.6%) and PMR (0.4% both) (figure 1).

Baseline characteristics of patients with and without MC are shown in table 3. Patients with post-STEMI MC were 10 years older and were more often women and hypertensive, with less prevalence of prior infarct. The use of reperfusion therapy was less frequent in patients who developed a MC (48.2% vs 75.0%; $P < .001$). Analyses by strata showed that among patients with MC, in the pre-PPCI period 48.5% received thrombolysis and the remaining 51.5% did not receive reperfusion treatment, whereas in the PPCI period only 4.5% received thrombolysis and 43.3% received PPCI reperfusion therapy. Logistic regression analysis modeling with the following covariates: age, gender, hypertension, previous myocardial infarction, infarct location and reperfusion were performed to compare prevalence of FWR in both periods. After multivariate adjustment, FWR prevalence remains higher in the first period compared to the PPCI period (OR, 1.93; 95%CI, 1.10-3.41; $P = .023$) (table 4).

Table 5 illustrates in-hospital characteristics and management of MC during the 2 studied periods.

Surgical repair increased in the PPCI period in all MC (7.4% vs 37.3%; $P < .001$), and this difference was statistically significant only for FWR (4.5% vs 34.6%; $P = .037$). Overall, higher 28-day mortality was observed in patients with MC treated conservatively in both periods (pre-PPCI: 79.4% vs 20.0%, $P = .012$; PPCI: 88.1% vs 24.0%; $P < .001$). Lower 28-day mortality has been observed in patients treated with cardiac surgery in the PPCI period of the FWR (90.0% vs 33.3%; $P < .004$) and PMR (75.0% vs 8.3%; $P = .027$), without significant differences neither in the pre-PPCI period nor in the VSR. The use of pericardial puncture in patients with FWR was similar in both periods (~45% of patients). Intra-aortic balloon pump had a limited use in the pre-PPCI group, although in the PPCI period was used in half of the patients with VSR and in one-third of those with PMR.

The 28-day mortality of all STEMI patients showed a relative reduction of 40% in the PPCI period (9.4% vs 5.6%; $P < .001$). Nevertheless, no significant changes in MC mortality as a whole were found, yet a trend was observed for PMR (table 2).

One-year mortality of all STEMI patients showed a relative reduction of 25% (10.9% vs 8.2%; $P < .001$) in the PPCI period. Although no relevant changes were found in PMR (62.5% vs 43.8%; $P = .386$), VSR (56.3% vs 81.8%; $P = .086$) or FWR (86.4% vs 75.9%; $P = .251$), comparing both periods (table 2).

DISCUSSION

The present study reports on a large series of post-STEMI MC spanning over 2 decades before (pre-PPCI: 1990-2000) and after the implementation of a PPCI reperfusion network (post-PPCI: 2007-2017).

Several findings may be highlighted. First, overall STEMI mortality has experienced a dramatic reduction both at 28 days and at 12 months. These data are in agreement with reports from other European regional networks.^{22,23} Second, development of post-STEMI MC declined in the PPCI period, mainly driven by a reduction of FWR (figure 1). Third, short-term mortality of the studied MC did not significantly benefit from more aggressive management with PPCI and cardiac surgery.

In this study, FWR was the only MC that showed significant prevalence decline with PPCI over thrombolysis. Early studies found a decrease in the prevalence of FWR with the early administration of fibrinolysis over no reperfusion, with the caveat that late fibrinolysis increased the rate of FWR.²⁴⁻²⁶

This latter association was speculated to be due to a major increase in the rate of myocardial hemorrhage. More recently, Puerto et al. reported MC in a cohort of elderly STEMI patients with mixed use of thrombolysis and PPCI and identified a 48% relative reduction in the incidence of FWR.²⁷ Here, we found a 60% relative reduction of FWR in the PPCI decade with universal use of PPCI compared to thrombolysis. In our series, a majority of patients in both periods obtained the benefit of reperfusion, which confers restoration of microvascular perfusion, limits the size of the myocardial infarction and the proportion of patients with transmural infarction, and favors the remodeling of the left ventricle.

Nevertheless, there are several possible explanations for the reduced prevalence of FWR in the PPCI period. First, the efficacy of thrombolysis to achieve TIMI grade 3 flow decreases when time to treatment increase, whereas PPCI has been shown to achieve infarct-related artery patency in > 90% of patients regardless of prehospital delays.²⁸ Accordingly, the increased patency rate associated with

1 PPCI may result in greater myocardial salvage and a reduced area of transmural infarction. Second,
2 animal studies have demonstrated that there is a greater amount of myocardial edema, hemorrhage,
3 and injury after reperfusion with thrombolytic therapy than with reperfusion by PPCI.²⁹
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6 There are few reports on the prevalence of VSR, as most studies combine FWR and VSR in the same
7 category under the name of “cardiac rupture”^{12,30} due to the low rate of VSR. Early registries including
8 information about the evolution of VSR showed a reduction trend in prevalence with thrombolysis
9 compared with no-reperfusion (0.2-0.3% vs 1-2%).^{15,31-33} In these studies a very low rate of PPCI was
10 observed: in the GUSTO-1 trial¹⁵ all patients received thrombolysis, in the MIDAS registry³¹ 19% of
11 patients were reperfused with PPCI, and in the GRACE registry³² 38% of patients were reperfused with
12 PPCI. The more contemporary APEX-AMI study³³, with a PPCI rate of 94%, found an incidence of VSR
13 of 0.17%, similar to previous data with thrombolysis. Collectively, these data indicate that the
14 incidence of VSR has declined with the use of reperfusion therapies, although the widespread use of
15 PPCI has failed to reduce this complication compared with thrombolysis, in line with the findings
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33 Several factors may contribute to the pathogenesis of VSR. At the biomolecular level, in the context of
34 reperfusion injury, VSR autopsy data reveal the presence of a myocardial hemorrhage in 83% of
35 patients treated with PPCI, in 71% of patients that received fibrinolysis, and in 18% of patients without
36 reperfusion therapy.³⁴ Previous studies have demonstrated that myocardial hemorrhage can create
37 dissections in the infarcted myocardium and delay the healing process. At the biophysical level, it is
38 known that the distribution of the mechanical load in the septum is different from that in the anterior
39 free wall, which could increase the stress on the infarcted area in the interventricular septum. Although
40 in-hospital prognosis is still ominous, the management with extracorporeal membrane oxygenation in
41 selective patients could be an option to improve prognosis.^{18, 35}
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54 The prevalence of PMR reported in the literature is so low that addressing PMR prevalence trends with
55 management changes remains elusive. Here we did not observe changes in PMR with thrombolysis or
56 PPCI. This fact could be due to a very low prevalence of PMR and that we only included confirmed
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1 papillary muscle ruptures after acute papillary muscle dysfunction was ruled out, since in the absence
2 of rupture conservative medical management is the best option with favorable evolution. Despite
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4 stable PMR prevalence rates in the 2 studied periods, PPCI together with a broader use of intra-aortic
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6 balloon pumps and cardiac surgery trend to improved survival at 12 months follow-up.
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9 The natural history of post-STEMI MC is catastrophic, and urgent surgical repair provides the best
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11 chance of survival in patients with MC. The present study shows increasing use of emergent surgery in
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13 the PPCI period, together with better medical management, but nonetheless the survival of these
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15 patients at 28 days and 12 months remains poor. Accordingly, there is an unmet need in the
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17 management of post-STEMI patients with MC. On one hand, preventing reperfusion injury might be a
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19 novel target in future adjunctive STEMI treatment to reduce inflammation and hemorrhage associated
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21 with it.³⁶ On the other, mechanical circulatory support, including ECMO, as a bridge to surgery, is being
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23 evaluated.³⁵ Such circulatory support could improve patients' hemodynamic condition allowing end-
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25 organ recovery during a few days before the surgical repair. The dark side of this is that VA-ECMO
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27 should not be extended more than 4-5 days, in order to prevent its hemorrhagic and thrombotic
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29 complications.
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34 35 36 37 **Study limitations**

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39 This study is not without limitations. It is an observational study, and therefore no causal relationships
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41 can be inferred. Despite being a single-center study based on a database designed and filled out
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43 prospectively (the Ruti-STEMI registry),⁴ our ICCU is the reference for acute cardiac care of patients in
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45 a wide area, with several community hospitals as a hub-and-spoke model. As such, this report provides
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47 epidemiological data on post-STEMI MC during 2 decades in a Mediterranean geographic area of
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49 ~850 000 inhabitants. The diagnostic criteria of acute myocardial infarction have been changed
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51 throughout the time of the study, especially due to the biochemical confirmation of myocardial
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53 infarction (CPK, CPK-MB, troponins and ultrasensitive troponins), which allow the detection of smaller
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55 infarcts. This fact could be very important in non-STEMI patient. In our STEMI registry, with very clear
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1 electrocardiogram criteria this fact could not be as relevant. We have only considered that MC with a
2 definitive diagnosis. Because of the period of the study and emergency situations, no MC was
3 diagnosed by computerized tomography or magnetic resonance imaging because these techniques
4 were not available. These factors could have led to a small underestimation of MCs. Finally, none of
5 the MCs reported here received mechanical circulatory support, as it was not available until more
6 recently.
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13 **CONCLUSIONS**

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16 Two decades were examined to better understand prevalence trends and outcomes of post-STEMI
17 MC. The establishment of regional PPCI networks has modified the landscape of MC in STEMI. Relative
18 to the pre-PPCI period, FWR declined by 60% in the PPCI era, likely due to greater myocardial salvage
19 and to PPCI reducing the area of transmural infarction. The prevalence of VSR and PMR remained
20 unchanged in the 2 studied decades. Despite increasing use of emergent surgery in the PPCI period,
21 28-day and 12-month mortality remain exceedingly high. Adjunctive cardioprotection against
22 reperfusion injury and mechanical support prior to surgery require further research if we are to
23 improve current sub-optimal results.
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40 **FUNDING**

41
42 None.
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47 **AUTHORS' CONTRIBUTIONS**

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49 All authors have contributed to the study according to international consensus on authorship and have
50 approved the final version.
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56 **CONFLICTS OF INTEREST**

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58 The authors have no relationship with industry related to this paper, and no disclosures.
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KEY POINTS

- What is known about the topic?

Most of the available data on the incidence and prognosis of post-STEMI MC come from classic studies that use thrombolysis as the only reperfusion or as the main method of reperfusion. These studies showed decreased FWR only with early administration of thrombolysis.

- What does this study add?

As the use of primary angioplasty has increased, the incidence of MC in patients with STEMI decreased over the past decade, primarily due to a reduction in FWR. But when MC has been developed, the short-term prognosis remains poor. More research is needed to improve MC outcome in STEMI patients. Cardioprotection against reperfusion injury and mechanical support should be studied to try to improve the current suboptimal results.

REFERENCES

1. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: Epidemiological update. *Eur Heart J*. 2014; 35: 2950-2959.
2. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation*. 2019;139:e56-e528.
3. Moran AE, Forouzanfar MH, Roth GA, et al. The global burden of ischemic heart disease in 1990 and 2010: the Global Burden of Disease 2010 study. *Circulation*. 2014;129:1493-1501.
4. García-García C, Oliveras T, Serra J, et al. Trends in Short- and Long-Term ST-Segment-Elevation Myocardial Infarction Prognosis Over 3 Decades: A Mediterranean Population-Based ST-Segment-Elevation Myocardial Infarction Registry. *J Am Heart Assoc*. 2020; 9: e017159.
5. Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction a population-based perspective. *Circulation*. 2009; 119: 1211-1219.
6. Sanborn TA, Sleeper LA, Bates ER, et al. Impact of thrombolysis, intra-aortic balloon pump counterpulsation, and their combination in cardiogenic shock complicating acute myocardial infarction: A report from the SHOCK Trial Registry. *J Am Coll Cardiol*. 2000; 36: 1123-1129.
7. Wayangankar SA, Bangalore S, McCoy LA, et al. Temporal trends and outcomes of patients undergoing percutaneous coronary interventions for cardiogenic shock in the setting of acute myocardial infarction. *JACC Cardiovasc Interv*. 2016;9:341-351.
8. García-García C, Oliveras T, El Ouaddi N, et al. Short- and Long-Term Mortality Trends in STEMI-Cardiogenic Shock over Three Decades (1989-2018): The Ruti-STEMI-Shock Registry. *J Clin Med*. 2020;9: 2398.
9. Figueras J, Cortadellas J, Calvo F, Soler-Soler J. Relevance of delayed hospital admission on development of cardiac rupture during acute myocardial infarction: Study in 225 patients with free wall, septal or papillary muscle rupture. *J Am Coll Cardiol*. 1998; 32: 135-139.

10. Reeder GS. Identification and Treatment of Complications of Myocardial Infarction. *Mayo Clin Proc.* 1995; 70: 880-884.
11. Lavie CJ, Gersh BJ. Mechanical and Electrical Complications of Acute Myocardial Infarction. *Mayo Clin Proc.* 1990; 65: 709-730.
12. Becker RC, Hochman JS, Cannon CP, et al. Fatal cardiac rupture among patients treated with thrombolytic agents and adjunctive thrombin antagonists: observations from the thrombolysis and thrombin inhibition in myocardial infarction 9 study. *J Am Coll Cardiol.* 1999; 33: 479-487.
13. Stevenson WG, Linssen GCM, Havenith MG, Brugada P, Wellens HJJ. The spectrum of death after myocardial infarction: A necropsy study. *Am Heart J.* 1989; 118: 1182-1188.
14. Pohjola-Sintonen S, Muller JE, Stone PH, et al. Ventricular septal and free wall rupture complicating acute myocardial infarction: experience in the Multicenter Investigation of Limitation of Infarct Size. *Am Heart J.* 1989; 117: 809-818.
15. Crenshaw BS, Granger CB, Birnbaum Y, et al. Risk factors, angiographic patterns, and outcomes in patients with ventricular septal defect complicating acute myocardial infarction. GUSTO-I (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) Trial Investigators. *Circulation.* 2000; 101:27.
16. Skehan JD, Carey C, Norrell MS, de Belder M, Balcon R, Mills PG. Patterns of coronary artery disease in post-infarction ventricular septal rupture. *Br Heart J.* 1989; 62: 268-272.
17. Prêtre R, Rickli H, Ye Q, Benedikt P, Turina MI. Frequency of collateral blood flow in the infarct-related coronary artery in rupture of the ventricular septum after acute myocardial infarction. *Am J Cardiol.* 2000;85:497-499.
18. Sánchez Vega JD, Alonso Salinas GL, Viéitez Flórez JM, et al. CIVIAM Study Investigators. Temporal trends in postinfarction ventricular septal rupture: the CIVIAM Registry. *Rev Esp Cardiol.* 2021;74:757-764.
19. Gunnar RM, Bourdillon PD, Dixon DW, et al. Medical / Scientific Statement Special Report ACC / AHA Guidelines for the Early Management of Patients With Acute Myocardial Infarction Association

1 Task Force on Assessment of Diagnostic and Therapeutic cardiovascular procedures. *Circulation*. 1990;
2 664-707.
3

4 20. Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients
5 presenting with ST-segment elevation. Task Force on the management of acute myocardial infarction
6 of the European Society of Cardiology. *Eur Heart J*. 2003; 24: 28-66.
7

8 21. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction
9 in patients presenting with ST-segment elevation. The task force on the management of ST-segment
10 elevation acute myocardial infarction of the European Society of Cardiology. *Eur Heart J*. 2012;
11 33:2569-2619.
12

13 22. Puymirat E, Simon T, Steg PG, et al. Association of Changes in Clinical Characteristics and
14 Management With Improvement in Survival Among Patients With ST-Elevation Myocardial Infarction.
15 *JAMA*. 2012; 308: 998-1006.
16

17 23. Gale CP, Allan V, Cattle BA, et al. Trends in hospital treatments, including revascularisation,
18 following acute myocardial infarction, 2003-2010: A multilevel and relative survival analysis for the
19 national institute for cardiovascular outcomes research (NICOR). *Heart*. 2014; 100: 582-589.
20

21 24. Gertz SD, Kragel AH, Kalan JM, Braunwald E, Roberts WC, The TIMI Investigators. Comparison of
22 coronary and myocardial morphologic findings in patients with and without thrombolytic therapy
23 during fatal first acute myocardial infarction. *Am J Cardiol*. 1990;66:904-909.
24

25 25. Honan MB, Harrell FE Jr, Reimer KA, et al. Cardiac rupture, mortality and the timing of thrombolytic
26 therapy: A meta-analysis. *J Am Coll Cardiol*. 1990; 16: 359-367.
27

28 26. Mauri F, De Biase AM, Franzosi MG, Pampallona S, Foresti A, Gasparini M. The Italian Group for the
29 Study of Streptokinase in Myocardial Infarct: analysis of intrahospital causes of death. *G Ital Cardiol*.
30 1987;17:37-44.
31

32 27. Puerto E, Viana-Tejedor A, Martínez-Sellés M, et al. Temporal Trends in Mechanical Complications
33 of Acute Myocardial Infarction in the Elderly. *J Am Coll Cardiol*. 2018; 72: 959-966.
34

28. Ellis SG, O'Neill WW, Bates ER, Walton JA, Nabel EG, Topol EJ. Coronary angioplasty as primary therapy for acute myocardial infarction 6 to 48 hours after symptom onset: Report of an initial experience. *J Am Coll Cardiol.* 1989; 13: 1122-1126.
29. Ohnishi Y, Butterfield MC, Saffitz JE, Sobel BE, Corr PB, Goldstein JA. Deleterious effects of a systemic lytic state on reperfused myocardium. Minimization of reperfusion injury and enhanced recovery of myocardial function by direct angioplasty. *Circulation.* 1995; 92:500-510.
30. Figueras J, Alcalde O, Barrabés JA, et al. Changes in hospital mortality rates in 425 patients with acute ST-elevation myocardial infarction and cardiac rupture over a 30-year period. *Circulation.* 2008; 118: 2783-2789.
31. Moreyra AE, Huang MS, Wilson AC, Deng Y, Cosgrove NM, Kostis JB; MIDAS Study Group (MIDAS 13). Trends in incidence and mortality rates of ventricular septal rupture during acute myocardial infarction. *Am J Cardiol.* 2010; 106: 1095-1100.
32. López-Sendón J, Gurfinkel EP, Lopez de Sa E, et al. Factors related to heart rupture in acute coronary syndromes in the global registry of acute coronary events. *Eur Heart J.* 2010; 31: 1449-1456.
33. French JK, Hellkamp AS, Armstrong PW, et al. Mechanical complications after percutaneous coronary intervention in ST-elevation myocardial infarction (from APEX-AMI). *Am J Cardiol.* 2010 Jan 1;105:59-63.
34. Honda S, Asaumi Y, Yamane T, et al. Trends in the clinical and pathological characteristics of cardiac rupture in patients with acute myocardial infarction over 35 years. *J Am Heart Assoc.* 2014;3:e000984.
35. Ariza-Solé A, Sánchez-Salado JC, Sbraga F, et al. The role of perioperative cardiorespiratory support in post infarction ventricular septal rupture-related cardiogenic shock. *Eur Heart J Acute Cardiovasc Care.* 2020;9:128-137.
36. Garcia-Dorado D, Théroux P, Solares J, et al. Determinants of hemorrhagic infarcts: Histologic observations from experiments involving coronary occlusion, coronary reperfusion, and reocclusion. *Am J Pathol.* 1990; 137: 301-311.

TABLES

Table 1. Demographic characteristics, medical therapies, and management of ST elevation myocardial infarction patients in the 2 studied periods

Characteristics	Pre-PPCI (N = 2250)	PPCI (N = 3783)	All Patients (N = 6033)	P
Age, mean years (SD)	60.4 (12.5)	62.4 (12.9)	61.7 (12.8)	< .001
Men	79.7	78.2	78.8	.177
Risk factors				
<i>Smoker</i>	44.3	43.6	43.8	.018
<i>Hypertension</i>	46.4	54.0	51.2	< .001
<i>Dyslipidemia</i>	40.8	57.1	51.0	< .001
<i>Diabetes mellitus</i>	26.4	25.1	25.6	.233
<i>Peripheral disease</i>	10.5	8.9	9.5	.046
Infarct features				
<i>Previous AMI</i>	18.3	11.7	14.1	< .001
<i>Anterior AMI</i>	42.5	46.1	44.8	< .001
<i>Killip-Kimball class^a</i>				
I	74.7	80.2	78.1	
II	10.6	10.3	10.4	
III	7.7	3.3	5.0	
IV	7.0	6.2	6.5	
<i>Reperfusion therapy</i>	49.7	89.1	74.4	< .001
Thrombolysis ^b	99.1	4.3	25.7	< .001
Primary PCI ^b	0.9	95.7	74.3	< .001
<i>Invasive VM</i>	7.6	7.1	7.2	.471
Medications				
<i>Aspirin</i>	92.5	97.8	94.7	.001
<i>Clopidogrel</i>	0.4	75.5	47.5	< .001
<i>Heparin</i>	64.6	54.7	58.4	< .001
<i>LMW heparin</i>	4.0	33.3	22.4	< .001
<i>Betablockers</i>	66.7	79.6	74.8	< .001
<i>Statins</i>	0.6	77.0	48.5	< .001
<i>ACE inhibitor/ARB</i>	24.4	49.2	39.9	< .001
STEMI Mortality				
<i>Early mortality^c</i>	8.4	4.2	5.8	< .001
<i>28-day mortality</i>	9.4	5.6	7.0	< .001
<i>1-year mortality</i>	10.9	8.2	9.2	< .001

^aMaximum Killip-Kimball class; ^bIn patients with reperfusion therapy; ^cMortality in the Intensive Cardiac Care Unit; ACE: angiotensin-converting enzyme; AMI: acute myocardial infarction; ARB: angiotensin

receptor blocker; LMW heparin: low-molecular-weight heparin; PCI: percutaneous coronary
intervention; PPCI, primary percutaneous coronary intervention.

Data are expressed as no. (%) or mean $\pm$ standard deviation.

Table 2. Prevalence, 28-days and 1-year mortality of post- ST elevation myocardial infarction mechanical complications

Variable	Prevalence			28-day mortality			1-year mortality		
	Pre-PPCI	PPCI	<i>P</i>	Pre-PPCI	PPCI	<i>P</i>	Pre-PPCI	PPCI	<i>P</i>
<i>Free wall rupture</i>	2.0 (44)	0.8 (29)	< .001	86.4 (38)	72.4 (21)	.139	86.4 (38)	75.9 (22)	0.251
<i>Ventricular septal rupture</i>	0.7 (16)	0.6 (22)	.538	56.3 (9)	81.8 (18)	.086	56.3 (9)	81.8 (18)	.086
<i>Papillary muscle rupture</i>	0.4 (8)	0.4 (16)	.688	50.0 (4)	25.0 (4)	.221	62.5 (5)	43.8 (7)	.386
<i>All MC</i>	3.0 (68)	1.8 (67)	< .001	75.0 (51)	64.2 (43)	.172	76.5 (52)	70.2 (47)	.406

MC: mechanical complication; PPCI: primary percutaneous coronary intervention.

Data are expressed as no. (%) or mean ± standard deviation.

Table 3. Baseline characteristics of patients with and without mechanical complications

Characteristics	MC (N = 135)	No MC (N = 5898)	P
Age, years	71.4 (9.4)	61.5 (12.7)	< .001
Women	37.0	20.9	< .001
Risk factors			
<i>Smoker</i>	50.4	70.8	< .001
<i>Hypertension</i>	60.0	51.0	.037
<i>Dyslipidemia</i>	37.0	51.3	< .001
<i>Diabetes mellitus</i>	26.7	25.6	.843
<i>Previous AMI</i>	9.6	14.2	< .001
Infarct features			
<i>Anterior wall AMI</i>	40.0	43.6	.410
<i>Killip III/IV</i>	58.8	10.4	< .001
<i>Reperfusion therapy</i>	48.2	75.0	< .001
Thrombolysis*	55.4	27.7	.170
PPCI*	44.6	72.3	< .001

*In patients with reperfusion therapy. AMI: acute myocardial infarction; MC: mechanical complications; PPCI: primary percutaneous coronary intervention.

Data are expressed as no. (%) or mean ± standard deviation.

Table 4. Logistic regression analysis for prevalence of free wall rupture between both periods

	OR	95%CI	P
<i>Age</i>	1.07	1.04-1.09	< .001
<i>Men</i>	0.59	0.35-0.99	.044
<i>Hypertension</i>	1.15	0.69-1.90	.589
<i>Previous AMI</i>	2.29	0.97-5.39	.058
<i>Anterior wall AMI</i>	0.81	0.50-1.32	.398
<i>Without reperfusion therapy</i>	2.67	1.54-4.65	< .001
<i>Pre-PPCI period</i>	1.93	1.10-3.41	.023

AMI: acute myocardial infarction; OR, odds ratio; PPCI: primary percutaneous coronary intervention.

Table 5. In-hospital characteristics and management of mechanical complications

Variable	Free wall rupture			Ventricular septal rupture			Papillary muscle rupture		
	Pre-PPCI	PPCI	<i>P</i>	Pre-PPCI	PPCI	<i>P</i>	Pre-PPCI	PPCI	<i>P</i>
<i>Killip III-IV</i>	27.2	50.0	.03	76.9	81.8	.26	83.3	87.6	.063
<i>Inotropes</i>	40.9	46.2	.71	76.9	72.7	.78	83.3	75	.68
<i>MV</i>	86.4	73.1	.26	15.4	4.5	.27	16.7	62.5	.056
<i>Pericardial puncture</i>	45.5	46.2	.96	---	---	---	---	---	---
<i>IABP</i>	---	---	---	7.7	50.0	.011	0	31.3	.12
<i>Cardiac surgery</i>	4.5	34.6	.037	15.4	22.7	.60	33.3	68.8	.18

IABP: intra-aortic balloon pump; MV: mechanic ventilation; PPCI: primary percutaneous coronary intervention.

Data are expressed as percentage (%).

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Figure 1. Central illustration. Prevalence of post-STEMI mechanical complications after the onset of a primary percutaneous coronary intervention network.

FWR: free-wall rupture; PMR: papillary muscle rupture; PPCI: primary percutaneous coronary intervention; VSR: ventricular septal rupture.

