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Performance analysis of a STEMI network: prognostic impact of first medical contact facility type

--Manuscript Draft--

Full Title:	Performance analysis of a STEMI network: prognostic impact of first medical contact facility type
Abstract:	<p>ABSTRACT</p> <p>Introduction and objectives: Delay in primary percutaneous coronary intervention (PPCI) in ST elevation myocardial infarction (STEMI) determines prognosis. Impact of first medical contact (FMC) facility type on reperfusion delays and mortality remains controversial.</p> <p>Methods: We performed a prospective registry of primary PCI-treated STEMI patients (2010-2020 period) in the Codi Infart STEMI network. We analysed 1-year all-cause mortality depending on the FMC facility type: emergency medical service (EMS), community hospital (CH), PCI-hospital (PCI-H) and primary care centre (PCC).</p> <p>Results: We included 18 332 patients (EMS 34.3%; CH 33.5%; PCI-H 12.3%; PCC 20.0%). Patients with Killip-Kimball classes III-IV were: EMS 8.43%, CH 5.54%, PCI-H 7.51%, PCC 3.76% ($P < .001$). All comorbidities and first medical assistance (FMA) complications were more frequent in EMS and PCI-H groups ($P < .05$) and less frequent in PCC group ($P < .05$ for most variables). PCI-H group had the shortest FMC-to-PCI delay (median 82 min); EMS group achieved the shortest total ischaemic time (median 151 min); CH had the longest reperfusion delays ($P < .001$). In an adjusted logistic regression model, PCI-H and CH groups were associated with higher 1-year mortality, OR, 1.22 (IC95% 1.00-1.48; $P = .048$), and OR, 1.17 (IC95% 1.02-1.36; $P = .030$) respectively, while PCC group was associated with lower 1-year mortality compared to EMS group, OR, 0.71 (IC95% 0.58-0.86; $P < .001$).</p> <p>Conclusions: FMC with PCI-H and CH was associated with higher adjusted 1-year mortality compared to FMC with EMS. PCC group had a much lower intrinsic risk and was associated with better outcomes despite longer revascularization delays.</p> <p>RESUMEN</p> <p>Introducción y objetivos: El tipo de primer contacto médico (PCM) en una red de angioplastia (ICPP) para el infarto con elevación del ST (IAMCEST) se asocia con diferentes grados de demora hasta ICPP y podría condicionar el pronóstico.</p> <p>Métodos: Registro de IAMCEST tratados con ICPP (2010-2020) en la red Codi Infart. Analizamos la mortalidad al año por cualquier causa según el tipo de PCM: servicio de emergencias médicas (SEM), hospital comarcal (HC), hospital de angioplastia (H-ICP) y centro de atención primaria (CAP).</p> <p>Resultados: Incluimos 18.332 pacientes (SEM 34,3%; HC 33,5%; H-ICP 12,3%; CAP 20,0%). La proporción de clases Killip III-IV fue: SEM 8,43%, HC 5,54%, H-ICP 7,51%, CAP 3,76% ($p < 0,001$). Comorbilidades y complicaciones en el PCM fueron más frecuentes en los grupos SEM y H-ICP ($p < 0,05$), y menores en el grupo CAP. El grupo H-ICP obtuvo el mejor tiempo PCM-ICPP (mediana 82 min); el grupo SEM consiguió el menor tiempo total de isquemia (mediana 151 min); el grupo HC obtuvo los mayores retrasos ($p < 0,001$). En un modelo de regresión logística ajustado, los grupos H-ICP y HC se asociaron con mayor mortalidad, OR = 1,22 (IC95% 1,00-1,48; $p = 0,048$) y OR = 1,17 (IC95% 1,02-1,36; $p = 0,030$) respectivamente, y el grupo CAP con menor mortalidad que el grupo SEM, OR = 0,71 (IC95% 0,58-0,86; $p < 0,001$).</p> <p>Conclusiones: el PCM con H-ICP y HC se asoció con mayor mortalidad ajustada a 1 año en comparación con el SEM. El grupo CAP se asoció con mejor pronóstico a pesar de reperfusión más tardías.</p>
Keywords:	<p>Keywords: Myocardial infarction. ST-elevation myocardial infarction (STEMI). Percutaneous coronary intervention. Transfer; Network. Treatment delay. Total ischaemic time.</p> <p>Palabras clave: Infarto de miocardio. Infarto con elevación del ST. IAMCEST. Intervencionismo coronario percutáneo. Retraso del sistema. Isquemia.</p>
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Corresponding Author:	Oriol de Diego, MD Clinic Barcelona Hospital University Barcelona, Barcelona SPAIN
First Author:	Oriol de Diego, MD
Order of Authors:	Oriol de Diego, MD Ferran Rueda Xavier Carrillo Teresa Oliveras Rut Andrea Nabil El Ouaddi Jordi Serra Carlos Labata Marc Ferrer Maria J. Martínez-Membrive Santiago Montero Josepa Mauri Joan García-Picart Sergio Rojas Albert Ariza Helena Tizón-Marcos Marta Faiges Mérida Cárdenas Rosa María Lidón Juan F Muñoz-Camacho Xavier Jiménez-Fàbrega Josep Lupón Antoni Bayés-Genís Cosme García-García
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Performance analysis of a STEMI network: prognostic impact of first medical contact facility type

Análisis de una red de atención al IAMCEST: impacto pronóstico del tipo de primer contacto médico

Oriol de DIEGO,^{a,b,c,*} Ferran RUEDA,^d Xavier CARRILLO,^d Teresa OLIVERAS,^d Rut ANDREA,^{a,b} Nabil El OUADDI,^d Jordi SERRA,^d Carlos LABATA,^d Marc FERRER,^d María J. MARTÍNEZ-MEMBRIVE,^d Santiago MONTERO,^d Josepa MAURI,^{d,f} Joan GARCÍA-PICART,^g Sergio ROJAS,^h Albert ARIZA,ⁱ Helena TIZÓN-MARCOS,^{j,k,e} Marta FAIGES,^l Mérida CÁRDENAS,^m Rosa María LIDÓN,^{n,e} Juan F. MUÑOZ-CAMACHO,^o Xavier JIMÉNEZ FÀBREGA,^p Josep LUPÓN,^{d,e, q} Antoni BAYÉS-GENÍS,^{d,e,q} and Cosme GARCÍA-GARCÍA,^{d,e,q} on behalf of the Codi Infart registry investigators[◊]

^a Servicio de Cardiología, Institut Clínic Cardiovascular, Hospital Clínic Barcelona, Barcelona, Spain

^b Institut D'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

^c Doctorando, Programa de doctorado, Departament de Medicina, Universitat Autònoma de Barcelona, Spain

^d Servicio de Cardiología, Institut del Cor, Hospital Universitari Germans Trias i Pujol, Badalona, Spain

^e Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV),

Spain ^f Servei Català de Salut, Generalitat de Catalunya, Registre del Codi Infart, Barcelona, Spain

^g Servicio de Cardiología, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

^h Servicio de Cardiología, Hospital Joan XXIII, Tarragona, Spain

ⁱ Servicio de Cardiología, Hospital Universitari de Bellvitge, Barcelona, Spain

^j Servicio de Cardiología, Hospital del Mar, Barcelona, Spain

^kHeart Diseases Biomedical Research Group, Instituto de investigaciones Hospital del Mar (IMIM), Barcelona, Spain

^lServicio de Cardiología, Hospital de Tortosa Verge de la Cinta, IISPV, Tarragona, Spain

^mServicio de Cardiología, Hospital Universitari Josep Trueta, Girona, Spain

ⁿServicio de Cardiología, Hospital Vall d'Hebron, Barcelona, Spain

^oServicio de Cardiología, Hospital Mútua de Terrassa, Terrassa, Barcelona, Spain

^pSistema d'Emergències Mèdiques, Barcelona, Spain

^qDepartamento de Medicina, Universidad Autónoma de Barcelona, Barcelona, Spain

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Corresponding author.

E-mail address: orioldediego@gmail.com (O. de Diego).

Twitter: @orioldediego @CosmeGarciacg7 @randreariba_rut

◊ A list of the investigators is available in the supplementary data.

ABSTRACT

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2 **Introduction and objectives:** Delay in primary percutaneous coronary intervention (PCI) in ST
3 elevation myocardial infarction (STEMI) determines prognosis. Impact of first medical contact (FMC)
4 facility type on reperfusion delays and mortality remains controversial.
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18 shortest FMC-to-PCI delay (median 82 min); EMS group achieved the shortest total ischaemic time
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25 **Conclusions:** FMC with PCI-H and CH was associated with higher adjusted 1-year mortality compared
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27 despite longer revascularization delays.
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31 intervention. Transfer; Network. Treatment delay. Total ischaemic time.
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2 **RESUMEN**
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11 *Introducción y objetivos:* El tipo de primer contacto médico (PCM) en una red de angioplastia (ICPP)
12 para el infarto con elevación del ST (IAMCEST) se asocia con diferentes grados de demora hasta ICPP y
13 podría condicionar el pronóstico.

14 *Métodos:* Registro de IAMCEST tratados con ICPP (2010-2020) en la red Codi Infart. Analizamos la
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18 La proporción de clases Killip III-IV fue: SEM 8,43%, HC 5,54%, H-ICP 7,51%, CAP 3,76% ($p < 0.001$).
19 Comorbilidades y complicaciones en el PCM fueron más frecuentes en los grupos SEM y H-ICP
20 ($p < 0.05$), y menores en el grupo CAP. El grupo H-ICP obtuvo el mejor tiempo PCM-ICPP (mediana
21 82 min); el grupo SEM consiguió el menor tiempo total de isquemia (mediana 151 min); el grupo HC
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Conclusiones: el PCM con H-ICP y HC se asoció con mayor mortalidad ajustada a 1 año en comparación
con el SEM. El grupo CAP se asoció con mejor pronóstico a pesar de reperfusiones más tardías.

Palabras clave: Infarto de miocardio. Infarto con elevación del ST. IAMCEST. Intervencionismo
coronario percutáneo. Retraso del sistema. Isquemia.

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2 **Abbreviations**
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Abbreviations

CH: community hospital
EMS: emergency medical services
PCC: primary care center
PCI-H: primary percutaneous coronary intervention hospital
PPCI: primary percutaneous coronary intervention
STEMI: ST elevation myocardial infarction

Abreviaturas

CAP: centro de atención primaria
HC: hospital comarcal
H-ICP: hospital con capacidad de intervencionismo coronario primario
IAMCEST: infarto con elevación del segmento ST
ICPP: intervencionismo coronario percutáneo primario
SEM: servicio de emergencias médicas

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2 **INTRODUCTION**
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INTRODUCTION

According to the European Society of Cardiology guidelines for the treatment of ST elevation myocardial infarction (STEMI), STEMI treatment should be facilitated by regional hospital networks, linked by an efficient and prioritized ambulance service to provide access to primary percutaneous coronary intervention (PPCI) expeditiously and effectively to as many patients as possible.¹

The STEMI network's efficiency is crucial because long delays to PPCI are associated with worse prognosis^{2,3}. Specifically, system delay (time from first medical contact [FMC] to reperfusion) has been proved to be related with mortality and it is also the most modifiable parameter.² Therefore, rapid diagnosis and transfer to the catheterization laboratory (cath lab) of a primary PCI-capable hospital (PCI-H) is important and should be optimized regardless of the prehospital pathway followed.

In a given STEMI network, diagnosis and, therefore, system activation permitting early transfer to the cath lab of the PPCI hospital can be made in different facility types (i.e., emergency medical services (EMS)' assistance "in the field", a community hospital [CH] a PCI-H or a primary care centre [PCC]), most of them requiring transfer to the PCI-H. The pathways determined by FMC facility type may be associated with different delays in reperfusion and, therefore, FMC with particular facility types may lead to better mortality results.

Previous studies mainly aimed to compare 2 different possible reperfusion pathways in STEMI (i.e., EMS vs direct admission to PCI-H, transfer from a CH vs direct admission to PCI-H...).^{4,5,6}

The present study sought to determine mortality results depending on FMC facility type considering all possible assistance pathways within our STEMI network. We evaluated a public healthcare system STEMI reperfusion network that aims to provide primary PCI to all STEMI cases of the region to determine if the pathways with shorter delays achieved lower mortalities than the ones with longer delays, to prioritize the former.

METHODS

The regional STEMI network Codi Infart was launched in June 2009. This network aimed to enhance reperfusion therapy for all STEMI cases in Catalonia, a 32 000 km² region with nearly 7.5 million inhabitants. To date, 11 hospitals in this region have gained PPCI capability. The Codi Infart network prioritizes PPCI as the first-choice reperfusion treatment, when the electrocardiogram-to-reperfusion time can be achieved in less than 120 min. The network is coordinated by the EMS, which also conducts all transfers. The Codi Infart network comprises 4 assistance pathways depending on the FMC facility in which the diagnosis is made: *a*) direct admission to a primary PCI-capable hospital (PCI-H); *b*) admission to a hospital or community hospital without PCI capability (CH); *c*) admission to a primary care centre or general practitioner centre (PCC); and *c*) EMS assistance and diagnosis “in the field” (EMS group). In the latter 3 groups, the EMS coordinates and carries out transfers from the FMC directly to the cath lab of a PCI-H (figure 1).

From the inception of the Codi Infart network, all cases have been recorded in a mandatory prospective multicentre registry maintained by the public health administration⁷, which has been described elsewhere^{8,9,10,11}. The stored data include demographic variables, previous medical history variables, clinical information at FMC such as Killip-Kimball class, potential medical complications in first medical assistance such as ventricular fibrillation, ventricular tachycardia, atrial fibrillation and atrioventricular block, location of the infarct (i.e., anterior, inferior, lateral), number of vessels affected, system-dependent factors, PCI and clinical data, and long-term all-cause mortality information.

For the present study, we selected all patients with confirmed STEMI (based on the criteria of ST elevation in FMC electrocardiogram determined by the physician of the FMC and confirmed by the physician of the PCI-H) that were treated with PPCI from January 2010 to December 2020. We excluded patients whose initial presentation was an out-of-hospital cardiac arrest, delayed arrivals (time from symptoms onset to FMC > 12 h), those already admitted to a hospital at symptoms onset, and those that resided outside the region (due to the inability to obtain follow-up information). Since information about presentation as an out-of-hospital cardiac arrest was only available from 2015, all patients with ventricular fibrillation at FMC were also excluded to eliminate the strongest potential selection bias

(out-of-hospital cardiac arrest are mainly assisted by EMS), and also considering that ventricular fibrillation could impact mortality more than reperfusion time.⁹ Patients that had received fibrinolysis at FMC were also excluded. Finally, subjects with invalid or missing values on classification variables, dates, time intervals or follow up information were excluded. Data regarding number of affected vessels only available since 2012 and data from certain baseline characteristics was only available for the last years.

Patients were grouped according to the FMC facility type (i.e., EMS, CH, PCI-H and PCC).

The primary end point was 1-year all-cause mortality. Secondary objectives included 30-day mortality, time from FMC to reperfusion, and total ischaemic time. Mortality data were based on official mortality registries from both Catalan and Spanish governments. The quality of data included in the registry is periodically verified by an external audit.

The FMC time with EMS was the moment the ambulance reached the patient, after the 112 call. For the rest of the groups, FMC was the time of arrival at the emergency department of each facility. For PCC, CH and PCI-H groups, patients mostly reached those facilities by themselves (especially in the case of PCCs), but they could also have been transferred by paramedical units of EMS or by EMS with non-diagnostic electrocardiogram, following the criteria of the EMS physician. In these 3 groups, system delay was considered equivalent to time from FMC to PCI. The time of EMS call was not available to calculate system delay for EMS group. Therefore, comparisons between groups were made using the FMC-to-PCI time, symptoms-to-FMC time and total ischaemic time.

All study procedures were in accordance with the Helsinki Declaration and Spanish data protection laws.

Statistical analysis

Categorical variables are presented as absolute and relative frequencies (%). Continuous variables are described as mean \pm standard deviation (SD) or as the median and interquartile range [IQR], when data

were not normally distributed. Clinical variables and reperfusion times were compared between groups with the *chi*-square test when normally distributed, for frequencies, and ANOVA was performed to compare means between more than two groups. Variables with non-normal distributions were compared with non-parametric tests (Mann Whitney or Kruskal-Wallis, as appropriate). *P*-values < .05 were considered statistically significant. A Cox-proportional hazards model was initially tested to analyse the relation of all-cause 1-year mortality with FMC facility type as the main independent variable (EMS group was set as reference). Nevertheless, proportional hazards assumption was not fulfilled for many important covariates (i.e., Killip class, sex, anterior STEMI) and, therefore, analyses were finally performed using multiple logistic regression. The model was adjusted with several covariates. Results are expressed as odds ratio (OR) and 95% confidence interval (95%CI). Furthermore, to better understand to what extent mortality differences between groups were explained by differences in reperfusion delays, total ischaemic time was also introduced in an additional model as a covariate.

Finally, a sensitivity analysis was conducted to assess the robustness of our data regarding the potential effect of the COVID-19 pandemics. For this purpose, we repeated the delays and mortality analysis on patients of years 2010-2019 and on patients of year 2020 separately.

All analyses were performed using Stata/IC 16.1 software (Stata Corp, College Station, United States).

RESULTS

We identified 23 963 patients accomplishing inclusion criteria from January 2010 to December 2020. Among these, 2 487 were excluded for presenting exclusion criteria and other 3 144 patients had missing or invalid values on the mentioned variables. Thus, we finally included 18 332 patients in the analysis (flowchart is shown in figure 2). Of those, 34.25% were attended by EMS on the field and directly transferred to the cath lab of a PCI-H, 33.47% were initially admitted to a CH, 12.28% were directly admitted to a PCI-H and 20.01% were initially assisted in a PCC.

1 Differences between groups regarding clinical characteristics and revascularization delays

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4 The groups had important differences in clinical characteristics (table 1) and reperfusion times
5 (table 2). The hospital-related groups (PCI-H and CH) had the highest proportions of women ($P = .010$)
6 and patients with diabetes ($P = .004$). Previous episodes of PCI, myocardial infarction, coronary artery
7 bypass grafting, and Killip-Kimball Classes III-IV were much common in the PCI-H and EMS groups.
8 The EMS group had the highest frequency of complications (ventricular tachycardia, atrial fibrillation,
9 atrioventricular block, need of intubation) that occurred during FMC assistance ($P < .001$ for most of
10 them, $P = .068$ for ventricular tachycardia). The PCC group had the lowest risk profile regarding
11 comorbidities and first medical assistance complications (lowest age, diabetes proportion, history of
12 PCI, myocardial infarction or coronary artery bypass grafting, lowest Killip-Kimball class, lowest
13 proportion of atrial fibrillation, intubation, and atrioventricular block in first medical assistance ($P < .05$
14 for all these variables).
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17 The shortest delay from FMC to reperfusion was observed in the PCI-H group (median 82 min,
18 $P < .001$), but the shortest total ischaemic time was achieved by the EMS group (median 151 min,
19 $P < .001$). The CH group had the longest reperfusion times (FMC-to-PCI delay 129 min, total ischaemic
20 time 238 min; $P < .001$ for both) (table 2, figure 3A-C).
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23 Mortality differences

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26 Crude 1-year all-cause mortality was higher in the PCI-H group (9.11%) and in the EMS group (8.60%)
27 than in the CH (8.25%) and PCC (4.77%) groups (log-rank test $P < .001$) (table 2, figure 4). In a logistic
28 regression model adjusting for covariates (i.e., age, sex, diabetes, previous acute myocardial infarction,
29 anterior location of STEMI, Killip-Kimball class, ventricular tachycardia in FMC) with EMS group set as
30 reference (because its shorter total ischaemic time), PCI-H (OR, 1.22; 95%CI 1.00-1.48; $P = .048$) and
31 CH (OR, 1.17; 95%CI 1.02-1.36; $P = .030$) groups were associated with higher 1-year mortality, while
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PCC group remained associated with lower 1-year mortality (OR, 0.71; 95%CI 0.58-0.86; $P = .001$) compared to EMS group. In an additional model adjusting also with total ischaemic time, mortality differences of PCI-H and CH groups compared to EMS group were attenuated and lost statistical significance (OR for CH was 1.09; 95%CI 0.94-1.27; $P = .254$ and OR for PCI-H was 1.17; 95%CI 0.97-1.43; $P = .109$), while mortality differences of PCC group compared to EMS slightly increased (OR, 0.67; 95%CI 0.55-0.81; $P < .001$).

Differences in 30-day mortality were less pronounced. Table 2 shows unadjusted 30-day mortality. In the logistic regression analysis adjusting for the same covariates, only a trend towards higher mortality was observed in CH and PCI-H groups in comparison to EMS group (OR, 1.13; 95%CI 0.94-1.36; $P = .203$ and OR, 1.18; 95%CI 0.92-1.51%; $P = .186$). Conversely, PCC group (OR, 0.73; 95%CI 0.57-0.94; $P = .014$) was associated with lower mortality compared to EMS group.

Impact of COVID-19 pandemics

When excluding patients from year 2020 and analysing patients from 2010-2019, an attenuation of adjusted mortality differences was observed. Crude 1-year mortality was 8.90% for EMS group, 7.99% for CH group, 9.30% for PCI-H group and 5.04% for PCC group. In the logistic regression analysis adjusting for the same covariates, mortality differences disappeared for CH (OR, 1.09; 95%CI, 0.94-1.27; $P = .268$) and only a trend towards higher mortality was observed for PCI-H (OR, 1.18; 95%CI, 0.97-1.44; $P = .106$), whereas PCC group persisted associated with lower 1-year mortality (OR 0.72; 95%CI, 0.59-0.89; $P = .002$) compared to EMS group.

Data from 2020 presented some differences in the profile of patients of each group compared to the previous period (table 3). A total of 1,877 patients were treated in 2020 (1871 in 2019), and group distribution was as follows: EMS 39.8%, CH 28.9%, PCI-H 9.32% and PCC 22.0%. In this period, and unlike the previous one, patients in CH group had a risk profile much similar to EMS group regarding Killip-Kimball class or complications at first medical assistance ($P = .038$ for Killip class). PCC group

1 persisted having the lowest risk profile patients. In 2020, time from symptoms onset to FMC was longer
2 but medians of FMC-to-reperfusion time did not differ from previous years (figure 3D), following the
3 same pattern described for the entire period: PCI-H with the shortest FMC-to-PCI time (78 min), EMS
4 with the shortest total ischaemic time (156 min) and CH with the longest reperfusion times (FMC-to-
5 PCI 120 min, total ischaemic time 238 min) ($P < .001$ for all of them; table 4). Unadjusted 1-year
6 mortality is shown in table 4. The logistic regression analysis showed, compared to EMS group, a higher
7 mortality in CH group (OR, 2.29; 95%CI, 1.41-3.73; $P = .001$), no significant differences in PCI-H group
8 (OR, 1.52; 95%CI, 0.70- 3.30; $P = .285$) and a trend towards lower mortality in PCC group (OR, 0.52;
9 95%CI, 0.25-1.09; $P = .084$). Table 5 shows the results of logistic regressions of all periods, for both 1-
10 year and 30-day mortality, and figure 5 summarizes the key findings of this study.
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DISCUSSION

27 The Codi Infart registry provided an excellent opportunity to examine the performance of a public
28 healthcare system STEMI network that covers an entire territory and, therefore, must attempt to offer
29 the fastest route to reperfusion to all inhabitants of the region, independently of the FMC facility type
30 and location. We evaluated the prognostic impact of the FMC facility type and the reperfusion delays
31 of the derived network pathways.
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39 The main finding of this study is that direct admission to a PCI-H and admission to CH and posterior
40 transfer to the PCI-H were associated with higher adjusted 1-year mortality compared to EMS
41 assistance “in the field” with direct transfer to the cath lab of the PCI-H. EMS group also achieved the
42 shortest total ischaemic time, and a FMC-to-reperfusion time not far from the PCI-H group one
43 (medians: 90 vs 82 min, respectively). These mortality differences, although weak, especially in the
44 case of PCI-H group ($P = .048$), were observed despite EMS group had the highest rate of complications
45 in first medical assistance, reflecting the much higher STEMI risk profile associated with EMS use, also
46 described in previous studies.^{12,13} Furthermore, the attenuation of these differences when adjusting
47 also by total ischaemic time supports that the mortality benefit of EMS group is at least partially driven
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1 by shorter reperfusion delays, especially compared to CH group, that experiences a largest attenuation
2 in the association when adding total ischaemic time to the model. On the other hand, PCC group was
3 associated with better 1-year outcome compared to EMS group despite longer delays (FMC-to-PCI
4 delay: 116 vs 90 min, total ischaemic time: 217 vs 151 min, respectively), a finding that could be
5 explained by the much lower risk profile in terms of patient baseline characteristics and STEMI risk in
6 the PCC group. Indeed, the higher mortality differences when adjusting also by total ischaemic time
7 support this hypothesis.

8
9 The fact that PCI-H group resulted associated with worse prognosis even though this group had the
10 shortest FMC-to-PCI delay deserves some comments. First, as represented in figure 3B, in patients with
11 FMC-to-PCI delay > 105 min of PCI-H and EMS groups (that is, 30% of patients of both groups), the
12 latter had, in fact, better results. Second, although system delay has classically been the focus of
13 attention as the most modifiable parameter and because its more linear relation with mortality for
14 being less influenced by selection biases, there is evidence enough to think that achieving a shorter
15 total ischaemic time should be a priority rather than focusing only on system delay.¹⁴ On this matter,
16 it is worth to note that part of the shorter total ischaemic time of EMS group is derived from providing
17 early assistance in the field and shortening the symptoms-to-FMC time (figure 3A), considered a
18 patient delay in the rest of pathways, but being, in fact, a system's responsibility. Third, patients of PCI-
19 H group had slightly worse baseline characteristics than those of EMS group, and this fact could have
20 contributed to the differences in 1-year mortality; indeed, this is endorsed by the lower change in
21 mortality differences when adjusting also by total ischaemic time.

22
23 The COVID-19 pandemics' impact on our analysis also needs to be discussed. Apparently, the benefit
24 on mortality in favour of EMS group is strongly related to the weight of 2020, since the analysis
25 excluding this year showed attenuation of the differences, especially with CH group, and since the
26 mortality benefit in year 2020 for EMS in comparison to CH group was remarkable. There are many
27 reasons for considering this year "unique", such as the longer symptoms-to-FMC delays, that could be
28 explained by the patients' fear of being admitted to a hospital, the lower proportions of STEMI treated
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1 during the first wave,¹⁵ or the modified risk profile distribution regarding FMC facilities, exemplified by
2 the higher proportions of Killip-Kimball classes III-IV in CH during this year. Nevertheless, time from
3 FMC to PCI was not significantly different from previous years,^{16,17} the number of patients treated
4 during the whole year was almost equal to that in 2019 and, most important, we cannot omit this year,
5 since it also reflects the performance of our healthcare system and because the pandemics or its
6 consequences are not over yet.
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9 In fact, the analysis of year 2020 provides valuable information that may contribute to a better
10 understanding of other results of the study: despite the logical benefit of improving PCI delays,
11 numerous studies have attempted to demonstrate that direct admission to a PCI-H and a transfer
12 "from the field" directly to the cath lab were associated with a better prognosis, compared to a
13 diagnosis and transfer from facilities without PCI capabilities; however, the results of those studies
14 were quite variable.^{4,5,18,19,20,21,22,23} The mortality benefit with the reduction of treatment delay proven
15 in studies comparing pre-hospital and in-hospital fibrinolysis^{24,25} is far more difficult to demonstrate in
16 the actual setting of PPCI²⁶ given that current studies remain subject to confounding and selection
17 biases inherent to registry data. Nevertheless, the COVID-19 pandemics actually modified the risk
18 profile associated to the CH group and made it more similar to that of EMS group. Therefore, the
19 resultant association of CH group with higher mortality in this period could be explained by having a
20 higher risk similar to those initially treated by the EMS but being associated with longer reperfusion
21 times. Conversely, patients of PCC group persisted presenting both the lowest risk baseline
22 characteristics and lowest Killip-Kimball class or complications. Hence, outcomes in this group were
23 probably less delay-dependant due to its intrinsic low mortality.¹³

24 The fact that differences between groups were much lower in 30-day than in 1-year mortality was an
25 expected finding considering that the benefit of a higher proportion of myocardial salvage by reduced
26 total ischaemic time does not only determine complications and mortality during admission but also
27 long-term complications; in addition, the lack of events due to a shorter follow-up period may partially
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1 justify the lower differences; therefore, it is likely that a longer period of time than 30 days is needed
2 to demonstrate this benefit.
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4 Regarding delays in reperfusion, EMS group irrefutably achieved the best results: it was associated
5 with a shorter symptoms-to-FMC time than the rest of groups, with a FMC-to-PCI delay not far from
6 PCI-H group and with the shortest total ischaemic time. Indeed, 50% of patients of this group achieved
7 a FMC-to-reperfusion time < 90 min. Concerning the shorter time from symptoms onset to FMC, and
8 considering that early presenters have been previously associated with worse outcomes,^{27,28} the good
9 demonstrated results of this pathway constitute a great opportunity to provide prompter
10 revascularization and improved prognosis to a high risk group. In contrast, only 40% of patients of CH
11 group had a system delay < 120 min. The present analysis should trigger more extensive studies about
12 sources of delay in PCC group but especially in CH group of the network to improve them. Therefore,
13 and taking into consideration the findings of this study, the use of EMS as FMC in STEMI should be
14 greatly potentiated bypassing the CH and PCC facilities. Thus, awareness-raising campaigns are needed
15 to tend to the higher rates (50-70%) of field-triage by EMS described in some studies.^{29,12,13} For that
16 purpose, it will be also necessary that the public administration supports logically and economically
17 this strategic objective of public health.
18

19 Our findings contribute to reinforce the pursuit of shorter total ischaemic times and not only focusing
20 on system delays, a goal that EMS can achieve better than any other FMC facility type. Moreover, our
21 study exemplifies how selection biases can hinder the association of clearly and directly related
22 parameters such as total ischaemic time and mortality, and deviate the focus and efforts to more bias-
23 free and measurable ones such as system delay. Perhaps more long-term strategies of public
24 awareness raise will be able to significantly reduce the forgotten components of total ischaemic time.
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29 **Limitations of the study** 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65

1 All observational and non-randomized studies are subjected to biases and our analysis is not free of
2 them. There might be additional characteristics not available for the present analysis that influenced
3 prognosis in our groups and whose absence partially justified the observed results³⁰. Second, the
4 exclusion of patients with missing data introduces a selection bias that cannot be corrected. Moreover,
5 the results during COVID-19 pandemics may also have additional interpretations. Finally, the variable
6 that determined if a patient was already admitted to a hospital at symptoms onset was only available
7 from 2015; the way and extent of impact of this only partial exclusion on our results is unknown to us.
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CONCLUSIONS

21 In this comprehensive, real-life evaluation of FMC facility type impact on prognosis and reperfusion
22 delays of a public healthcare system STEMI network, FMC with EMS was associated with shorter total
23 ischaemic time than any other pathway, accounting for higher adjusted 1-year mortality in PCI-H and
24 CH groups compared to EMS. FMC with primary care centres, despite longer reperfusion delays,
25 resulted associated with better outcomes, probably because the intrinsic low risk characteristics of this
26 group of patients. Public awareness-raising campaigns are required to reduce patient delay and
27 emphasize the need of contacting the EMS when facing MI-compatible symptoms.
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AUTHORS' CONTRIBUTIONS

47 O. de Diego takes responsibility for all aspects of the reliability and lack of bias of the data and their
48 discussion. O. de Diego: data collection, statistical analysis, manuscript elaboration, final approval.
49
50 C. García-García, J. Lupón, F. Rueda, X. Carrillo, R. Andrea: data collection, contributions to statistical
51 analysis and manuscript elaboration, final approval.
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1 T. Oliveras, N. El Ouadji, J. Serra, C. Labata, M. Ferrer, M. J. Martínez-Membrive, S. Montero, J.
2 Mauri, J. García-Picart, S. Rojas, A. Ariza, H. Tizón-Marcos, M. Faiges, M. Cárdenas, R. M. Lidón, J. F.
3
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5 manuscript, final approval.
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10 **CONFLICTS OF INTEREST**
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12 This research work has no relationships with industry.
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17 **KEY POINTS**
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21 **WHAT IS KNOWN ABOUT THE TOPIC?**
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24 Many studies have assessed the mortality impact of the type of FMC in STEMI networks by comparing
25 2 different options (mainly FMC with EMS vs direct admission to a PCI hospital and direct admission to
26 a PCI hospital vs interhospital transfer) but a direct comparison of all possible pathways in a given
27 STEMI network is necessary to improve its performance.
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33 **WHAT DOES THIS STUDY ADD?**
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36 We found that STEMI patients assisted by EMS as FMC achieved shorter total ischaemic times than in
37 any other pathway, not only by shortening FMC-to-PCI time but also being the only circuit that
38 shortened the symptoms-to-FMC delay. FMC with EMS was associated with better 1-year outcomes
39 than direct admission to a PCI hospital or FMC to a community hospital. A profound analysis of STEMI
40 networks performance and public healthcare strategies should be endorsed to achieve a reduction of
41 all components of treatment delay of STEMI and to optimize all possible pathways by potentiating EMS
42 as FMC and improving the slower circuits.
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FIGURE LEGENDS

Figure 1. Codi Infart STEMI network in Catalonia. **A.** Codi Infart pathways; **B.** Codi Infart operation area and 11 involved PCI-capable hospitals. Cath Lab: catheterization laboratory; CH: community hospital; EMS: emergency medical service; FMC: first medical contact; PCC: primary care centre; PCI-H: hospital with PCI-capability.

Figure 2. Flowchart shows patient inclusion and exclusion process. OHCA, out of hospital cardiac arrest; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; VF, ventricular fibrillation.

Figure 3. Reperfusion delays. **A.** Cumulative frequencies of symptoms-to-FMC delay depending on FMC facility type. **B.** Cumulative frequencies of FMC-to-PCI delay depending on FMC facility type. **C.** Cumulative frequencies of total ischaemic time depending on FMC facility type. **D.** Median symptoms-to-FMC and FMC-to-PCI delays over years (in the global population). FMC, first medical contact; PCI, primary coronary intervention.

Figure 4. Kaplan-Meier survival curves depending on first medical contact facility type. PCI, primary coronary intervention.

Figure 5. Central illustration. Impact of first medical contact facility type on ischaemia time and 1-year mortality. CH, community hospital; EMS, Emergency Medical Services; PPCI, primary percutaneous coronary intervention; PCC, primary care centre; PCI-H, primary percutaneous coronary intervention hospital; STEMI, ST elevation myocardial infarction.

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Table 1. Baseline and clinical characteristics. Patients from 2010-2020

Characteristics	Emergency medical services (n = 6278)	Community hospital (n = 6135)	PCI hospital (n = 2251)	Primary Care Centre (n = 3668)	Total (n = 18332)	P for global differences
<i>Age, years</i>	64.6 (13.1)	63.8 (13.3)	63.8 (13.2)	62.9 (13.2)	63.3 (13.2)	< .001
<i>Men</i>	4949 (78.7)	4730 (77.1)	1743 (77.4)	2926 (79.8)	14 339 (78.2)	.010
<i>Diabetes mellitus</i>	1282 (20.4)	1339 (21.8)	529 (23.5)	739 (20.2)	3889 (21.2)	.004
<i>Previous AMI</i>	712 (11.3)	535 (8.7)	280 (12.4)	209 (5.7)	1736 (9.5)	< .001
<i>Previous PCI</i>	680 (10.8)	461 (7.5)	253 (11.2)	177 (4.8)	1571 (8.6)	< .001
<i>Previous CABG</i>	73 (1.2)	54 (0.9)	29 (1.3)	15 (0.4)	171 (0.9)	< .001
<i>Complications during FMC</i>						
Intubation	88 (1.5)	39 (0.7)	24 (1.2)	14 (0.4)	165 (1.0)	< .001
Ventricular tachycardia	52 (0.9)	42 (0.7)	9 (0.4)	27 (0.7)	137 (0.8)	.068
Atrial fibrillation	93 (1.5)	59 (1.0)	8 (0.8)	21 (0.6)	191 (1.0)	< .001
AV block	415 (6.6)	232 (3.8)	94 (4.2)	102 (2.8)	843 (4.6)	< .001
<i>Killip-Kimball Class</i>						
I	5273 (84.0)	5349 (87.2)	1927 (85.6)	3263 (89.0)	15 812 (83.6)	< .001
II	476 (7.6)	446 (7.3)	155 (6.9)	267 (7.3)	1344 (7.3)	
III	119 (1.9)	107 (1.7)	54 (2.4)	35 (1.0)	315 (1.7)	
IV	410 (6.5)	233 (3.8)	115 (5.1)	103 (2.8)	861 (4.7)	
<i>AMI location</i>						
Anterior wall	2644 (42.1)	2533 (41.3)	897 (39.9)	1523 (41.5)	7597 (41.4)	.308
Inferior wall	3099 (49.4)	3028 (49.4)	1086 (48.3)	1819 (49.6)	9032 (49.3)	.768
Lateral wall	630 (10.0)	698 (11.4)	258 (11.5)	439 (12.0)	2025 (11.1)	.013
<i>Affected coronary arteries</i>						
3 vessel disease (n = 15 301)	670 (12.5)	751 (15.1)	262 (14.6)	382 (12.1)	2065 (13.5)	< .001
Left main disease (n = 15 476)	168 (3.1)	154 (3.1)	61 (3.4)	62 (2.0)	445 (2.9)	.005

PCI, primary coronary intervention; AMI, acute myocardial infarction; CABG, coronary-aortic bypass grafting; FMC, first medical contact; SD, standard deviation; COPD, chronic obstructive pulmonary disease.

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Values are expressed as no. (%).

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Table 2. Delays to reperfusion and mortality depending on first medical care facility type. Patients
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Characteristics	Emergency medical services (n = 6,278)	Community hospital (n = 6,135)	PCI hospital (n = 2,251)	Primary Care Centre (n = 3,668)	Total (n = 18,332)	P for global differences
<i>Treatment delays, min</i>						
Symptoms onset-to-FMC time	52 [30-100]	88 [42-180]	95 [44-190]	85 [39-180]	70 [35-150]	< .001
FMC-to-PCI time	90 [74-113]	129 [104-170]	82 [60-116]	116 [95-146]	107 [84-140]	< .001
Total ischaemic time	151 [119-210]	238 [170-355]	193 [126-310]	217 [155-325]	195 [140-295]	< .001
<i>Mortality</i>						
1-year mortality	540 (8.60)	506 (8.25)	205 (9.11)	175 (4.77)	1426 (7.78)	< .001
30-day mortality	332 (5.29)	290 (4.73)	123 (5.46)	102 (2.78)	847 (4.62)	< .001

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34 PCI, primary coronary intervention; FMC, first medical contact.
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Values are expressed as no. (%), or median [interquartile range].

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Table 3. Baseline and clinical characteristics. Patients from year 2020

Characteristics	Emergency medical services (n = 747)	Community hospital (n = 542)	PCI hospital (n = 175)	Primary Care Centre (n = 413)	Total (n = 1,877)	P for global differences
<i>Age, years</i>	64.1 (13.0)	63.5 (13.0)	62.8 (12.0)	63.0 (13.0)	63.6 (12.9)	.444
<i>Men</i>	601 (80,5)	435 (80.3)	143 (81.7)	337 (81.6)	1,516 (78.2)	.936
<i>Diabetes mellitus</i>	157 (21.0)	140 (25.8)	42 (24.0)	87 (21.1)	426 (22.7)	.170
<i>Previous AMI</i>	90 (12.1)	45 (8.3)	24 (13.7)	17 (4.1)	176 (9.4)	< .001
<i>Previous PCI</i>	86 (11.5)	37 (6.8)	29 (16.6)	15 (3.6)	167 (8.9)	< .001
<i>Previous CABG</i>	10 (1.3)	4 (0.7)	1 (0.6)	0 (0)	15 (0.8)	.102
<i>Complications during FMC</i>						
Intubation	6 (0.8)	5 (0.9)	0 (0)	1 (0.2)	165 (0.6)	.369
Ventricular tachycardia	9 (1.2)	2 (0.4)	1 (0.6)	3 (0.7)	15 (0.8)	.398
Atrial fibrillation	10 (1.3)	2 (0.4)	0 (0)	2 (0.5)	14 (0.8)	.099
AV block	36 (4.8)	23 (4.2)	3 (1.7)	10 (2.4)	72 (3.8)	.087
<i>Killip-Kimball Class</i>						
I	640 (85.7)	462 (85.2)	150 (85.7)	358 (86.7)	1,610 (85.8)	.038
II	51 (6.8)	45 (8.3)	15 (8.6)	42 (10.2)	153 (8.2)	
III	14 (1.8)	5 (0.9)	5 (2.8)	3 (0.7)	27 (1.4)	
IV	42 (5.6)	30 (5.5)	5 (2.8)	10 (2.4)	87 (4.6)	
<i>AMI location</i>						
Anterior wall	436 (41.6)	303 (44.1)	109 (37.7)	238 (42.4)	1,086 (42.1)	.504
Inferior wall	375 (50.2)	254 (46.9)	94 (53.7)	208 (50.4)	931 (49.6)	.390
Lateral wall	74 (9.9)	70 (12.9)	17 (9.7)	51 (12.4)	212 (11.3)	.290
<i>Affected coronary arteries</i>						
3 vessel disease	91 (12.2)	87 (16.2)	19 (10.9)	47 (11.4)	244 (13.1)	.082
Left main disease	23 (3.1)	14 (2.6)	4 (2.3)	7 (1.7)	48 (2.6)	.552

PCI, primary coronary intervention; AMI, acute myocardial infarction; CABG, coronary-aortic bypass grafting; FMC, first medical contact; SD, standard deviation.

Values are expressed as no. (%).

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2 **Table 4. Delays to reperfusion and mortality depending on FMC facility type during year 2020**
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Characteristics	Emergency medical services (n = 747)	Community hospital (n = 542)	PCI hospital (n = 175)	Primary care centre (n = 413)	Total (n = 1,877)	P for global differences
<i>Treatment delays</i>						
Symptoms onset-to-FMC time	59 [30-113]	90 [45-181]	109 [46-205]	108 [47-211]	79 [37-165]	< .001
FMC-to-PCI time	90 [73-110]	120 [99-158]	78 [60-107]	112 [93-135]	102 [82-130]	< .001
Total ischaemic time	156 [120-225]	238 [167-358]	204 [124-335]	233 [158-346]	195 [137-297]	< .001
<i>Mortality</i>						
1-year mortality	48 (6.43)	59 (10.89)	12 (6.86)	11 (2.66)	130 (6.93)	< .001
30-day mortality	30 (4.02)	33 (6.09)	7 (4.00)	5 (1.21)	75 (4.00)	.002

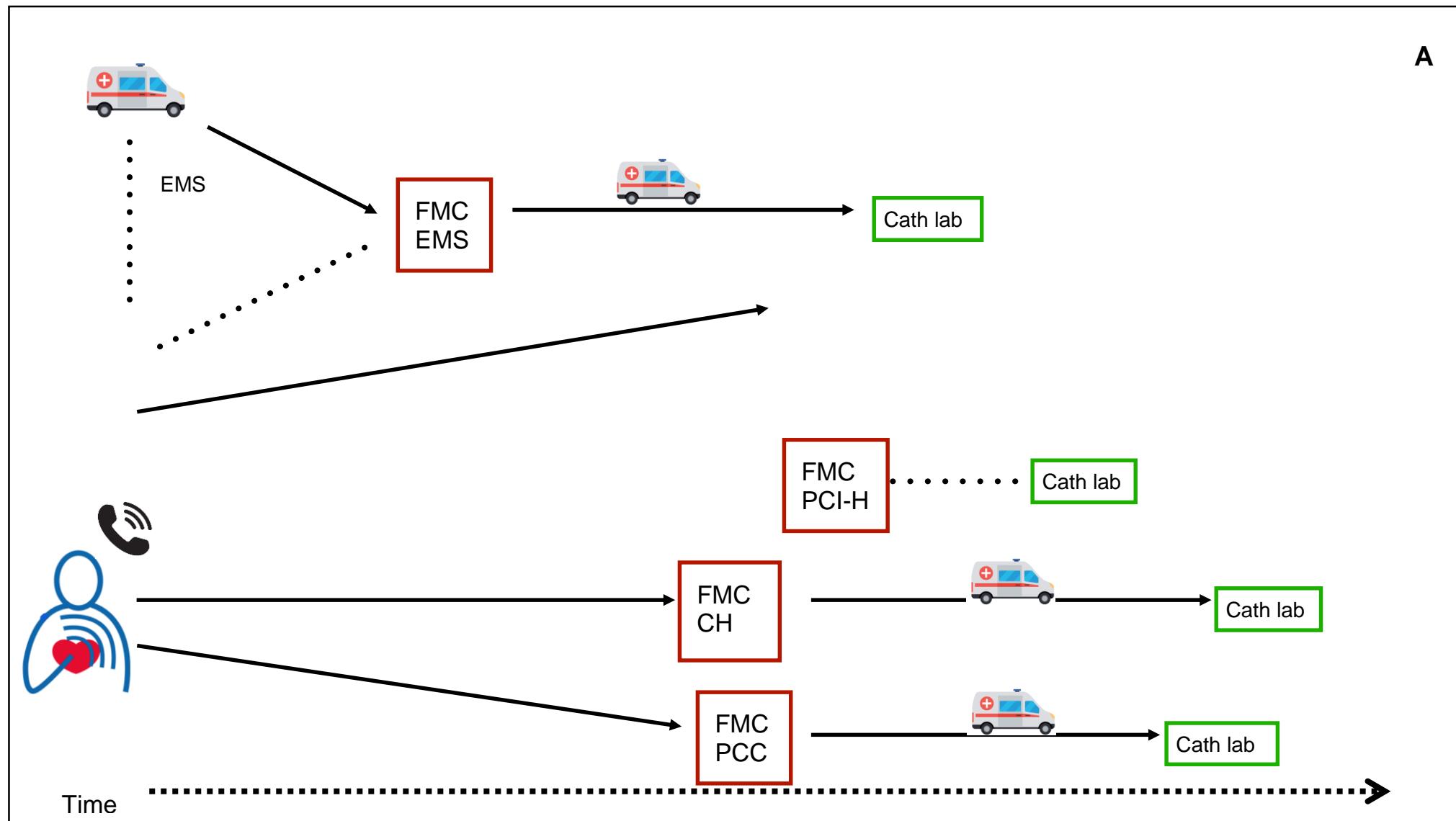
27 FMC, first medical contact; PCI, percutaneous coronary intervention.
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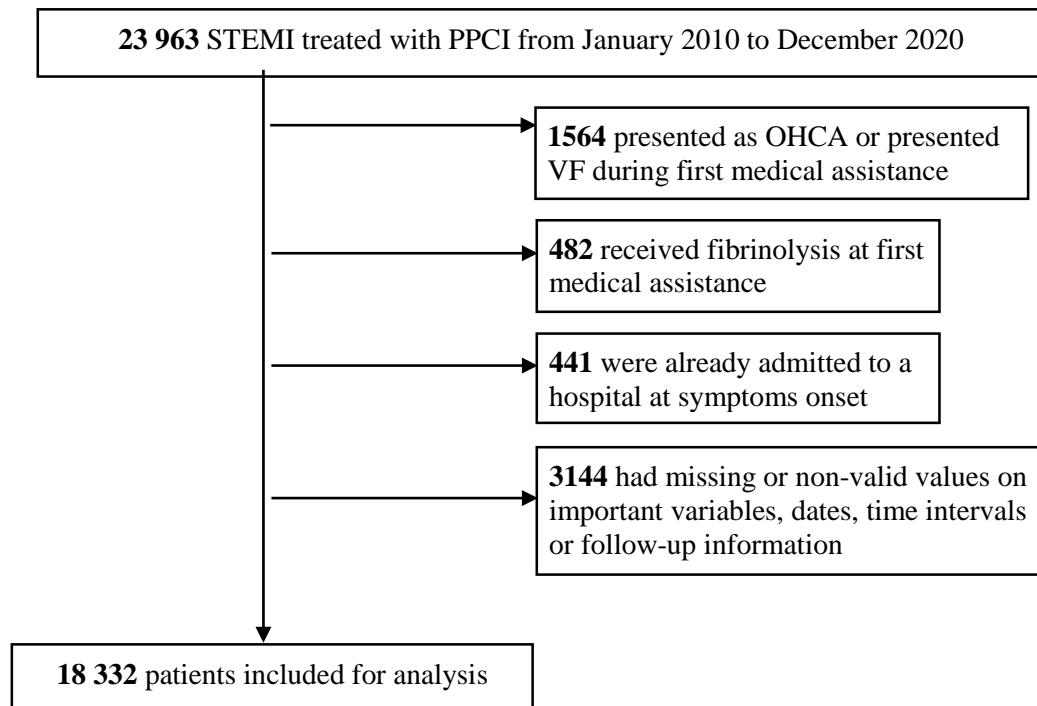
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31 Values are expressed as no. (%), or median [interquartile range].
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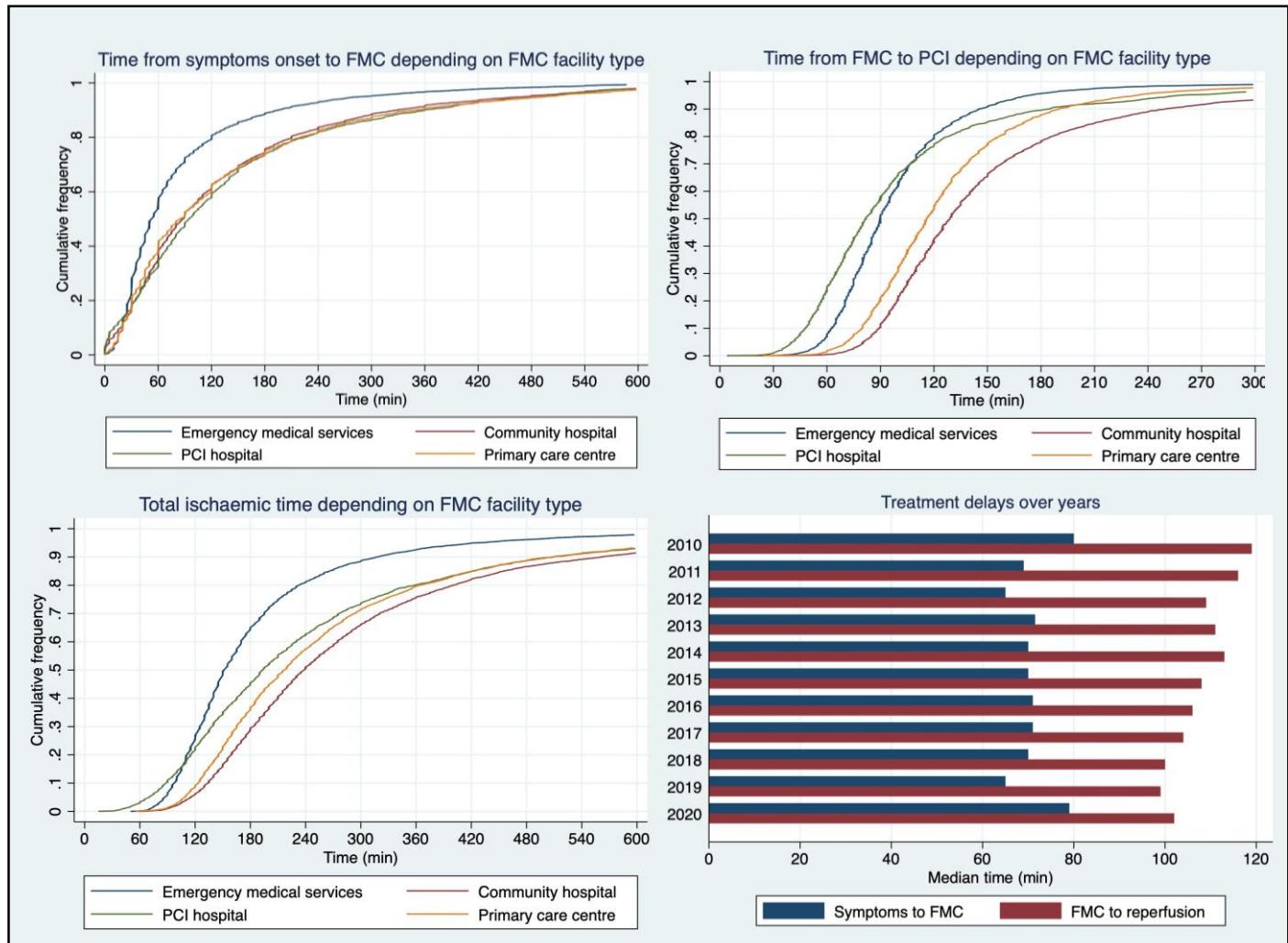
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2 **Table 5. Multiple logistic regressions for 30-day and 1-year mortality in the full period, in 2010-**
3 **2019 and in 2020**
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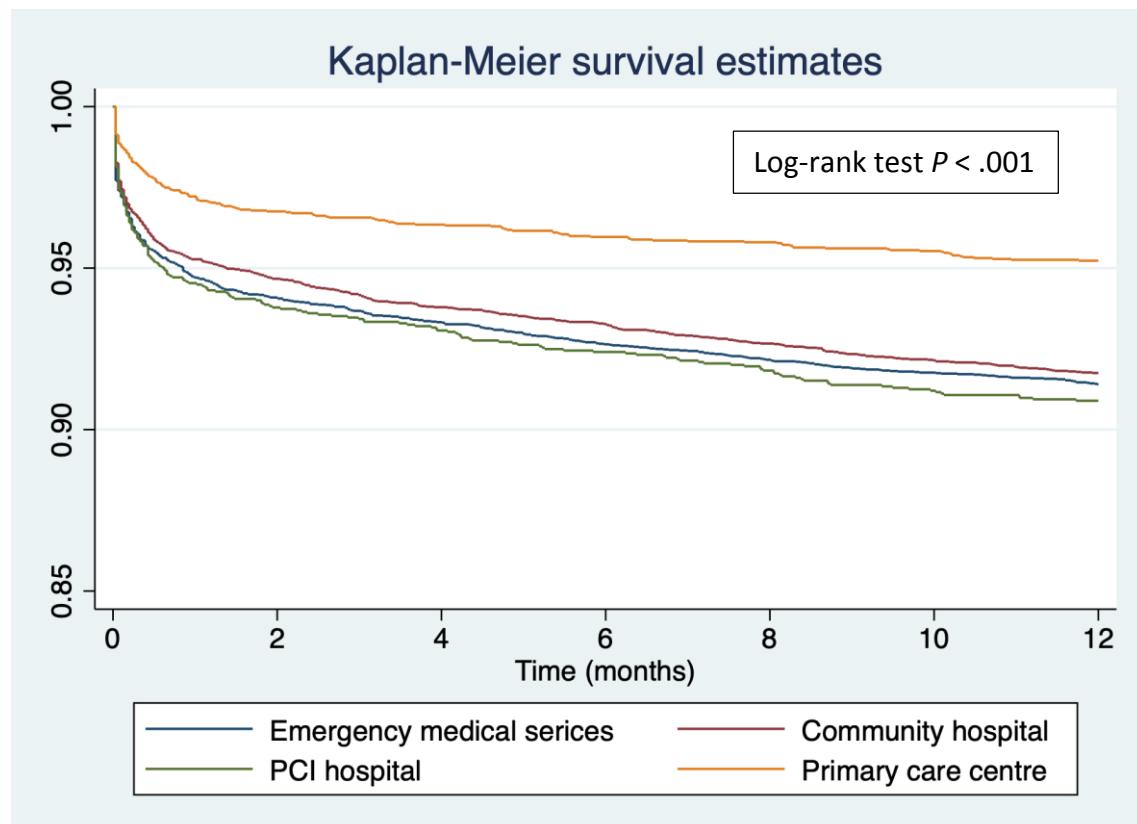
	Full period		2010-2019		2020	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
<i>1-year mortality</i>						
CH group	1.17 (1.02-1.36)	.030	1.09 (0.94-1.27)	.268	2.29 (1.41-3.73)	.001
PCI-H group	1.22 (1.00-1.48)	.048	1.18 (0.97-1.44)	.106	1.52 (0.70-3.30)	.285
PCC group	0.71 (0.58-0.86)	< .001	0.72 (0.59-0.89)	.002	0.52 (0.25-1.09)	.084
<i>30-day mortality</i>						
CH group	1.13 (0.94-1.36)	.203	1.06 (0.87-1.29)	.567	2.12 (1.11-4.06)	.023
PCI-H group	1.18 (0.92-1.51)	.186	1.15 (0.89-1.48)	.293	1.52 (0.54-4.31)	.431
PCC group	0.73 (0.57-0.94)	.014	0.76 (0.59-0.98)	.037	0.43 (0.14-1.25)	.120

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25 Reference group: EMS. Adjusted for covariates: age, sex, diabetes, previous acute myocardial
26 infarction, anterior location of STEMI, Killip-Kimball class (as categorical variable with 4 categories with
27 Killip I as reference) and ventricular tachycardia in first medical assistance. CI, confidence interval; EMS,
28 emergency medical service; FMA, first medical assistance; OR, odds ratio; PCC, primary care centre;
29 PCI-H, Hospital with percutaneous coronary intervention capability; STEMI, ST elevation myocardial
30 infarction; VT, ventricular tachycardia.
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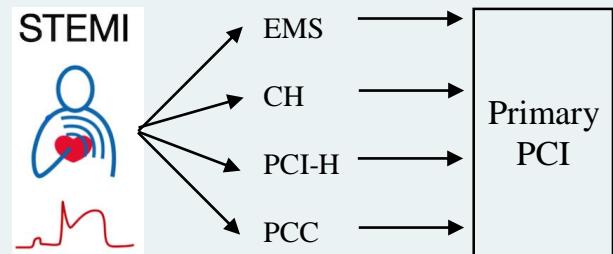




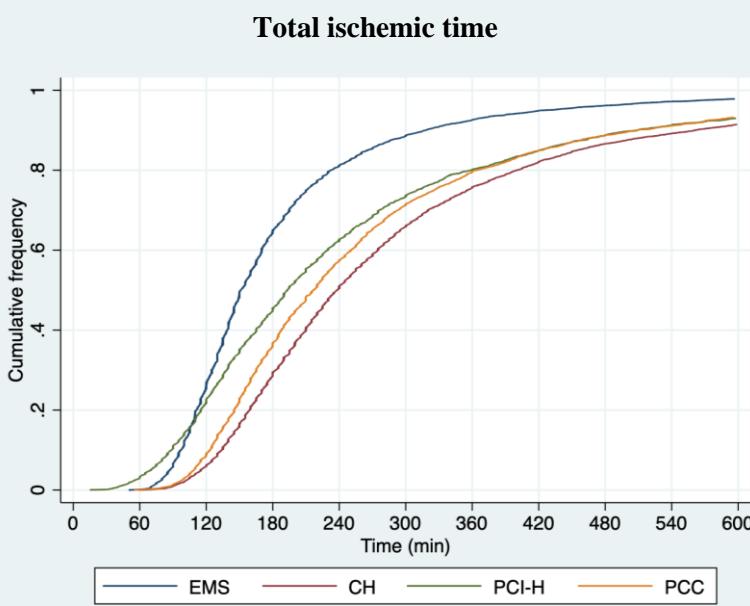


BACKGROUND AND PURPOSE

- EMS diagnosis on the field and direct transfer to the cath lab has been associated with shorter reperfusion delays and improved mortality in PPCI-treated STEMI patients
- Regional STEMI network registry (2010-2020): 18 332 patients included. We analyzed reperfusion delays and mortality depending on the pathway defined by each FMC facility type in our network.



RESULTS

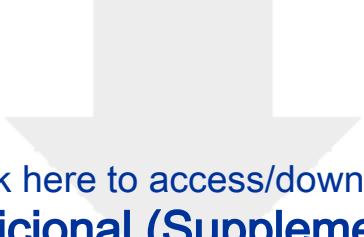


Adjusted 1-year mortality

- EMS: reference
- CH: OR, 1.17; 95%CI, 1.02-1.36
- PCI-H: OR, 1.22; 95%CI, 1.00-1.48
- PCC: OR, 0.71; 95%CI, 0.58-0.86
- Mortality differences in CH and PCI-H groups compared to EMS group resulted attenuated and lost statistical significance when adjusting also by total ischemic time, while differences between PCC and EMS were emphasized.

CONCLUSIONS

- Direct admission to PCI-H and admission to CH and posterior transfer for PCI were associated with higher 1-year mortality compared to EMS assistance in the field with direct transfer to the cath lab. These differences were partially driven by shorter reperfusion delays in EMS group.



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Material adicional (Supplementary data)
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