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Original article

Regional differences in STEMI care in Spain. Data from the ACI-SEC Infarction Code Registry

Oriol Rodríguez-Leor,[a,b,c,*] Ana Belén Cid-Álvarez,[d] Raúl Moreno,[b,e] Xavier Rosselló,[b,f,g] Soledad Ojeda,[h] Ana Serrador,[b,i] Ramón López-Palop,[j] Javier Martín-Moreiras,[b,k] José Ramón Rumoroso,[l] Ángel Cequier,[m] Borja Ibáñez,[b,f,n] Ignacio Cruz-González,[b,k] Rafael Romaguera,[m] Sergio Raposeiras,[o] and Armando Pérez de Prado[p] on behalf of the investigators from the Infarction Code Working Group of the ACI-SEC[◊]

[a] *Institut del Cor, Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona, Spain*
[b] *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[c] *Institut de Recerca en Ciències de la Salut Germans Trias i Pujol, Badalona, Barcelona, Spain*
[d] *Servicio de Cardiología, Hospital Clínico de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[e] *Servicio de Cardiología, Hospital Universitario La Paz, Madrid, Spain*
[f] *Laboratorio Traslacional para la Imagen y Terapia Cardiovascular, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain*
[g] *Servicio de Cardiología, Institut d'Investigació Sanitària Illes Balears (IdISBa), Hospital Universitari Son Espases, Palma de Mallorca, Islas Baleares, Spain*
[h] *Servicio de Cardiología, Hospital Universitario Reina Sofía, Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Universidad de Córdoba, Córdoba, Spain*
[i] *Servicio de Cardiología, Hospital Clínico de Valladolid, Valladolid, Spain*
[j] *Servicio de Cardiología, Hospital Clínico Universitario Virgen de la Arrixaca, El Palmar, Murcia, Spain*
[k] *Servicio de Cardiología, Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Salamanca, Spain*
[l] *Servicio de Cardiología, Hospital de Galdakao-Usansolo, Galdakao, Vizcaya, Spain*
[m] *Servicio de Cardiología, Hospital de Bellvitge - IDIBELL, Universitat de Barcelona, L'Hospitalet de Llobregat, Barcelona, Spain*
[n] *Servicio de Cardiología, IIS-Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*
[o] *Servicio de Cardiología, Hospital Universitario Álvaro Cunqueiro, Instituto de Investigación Sanitaria Galicia Sur, Vigo, Pontevedra, Spain*
[p] *Servicio de Cardiología, Hospital de León, León, Spain*

ABSTRACT

Introduction and objectives: Geographical and organizational differences between different autonomous communities (AC) can generate differences in care for ST-segment elevation myocardial infarction (STEMI). A total of 17 heart attack code programs have been compared in terms of incidence rate, clinical characteristics, reperfusion therapy, delay to reperfusion, and 30-day mortality.
Methods: National prospective observational study (83 centers included in 17 infarction networks). The recruitment period was 3 months (April 1 to June 30, 2019) with clinical follow-up at 30 days.
Results: 4366 patients with STEMI were included. The incidence rate was variable between different AC ($P < .0001$), as was gender ($P = .003$) and the prevalence of cardiovascular risk factors ($P < .0001$). Reperfusion treatment was primary angioplasty (range 77.5%-97.8%), fibrinolysis (range 0%-12.9%) or no treatment (range 2.2%- 13.5%). The analysis of the delay to reperfusion showed significant differences ($P < .001$) for all the intervals analyzed. There were significant differences in 30-days mortality that disappeared after adjusting for clinical and healthcare network characteristics.
Conclusions: Large differences in STEMI care have been detected between the different AC, in terms of incidence rate, clinical characteristics, reperfusion treatment, delay until reperfusion, and 30-day mortality. The differences in mortality disappeared after adjusting for the characteristics of the patient and the care network.

Keywords: STEMI. Population characteristics. Angioplasty.

[◊] The investigators, centers, and organizations involved in the Infarction Code Working Group of the Interventional Cardiology Association of the Spanish Society of Cardiology are shown on the supplementary data.

*** Corresponding author.**
E-mail address: oriolrodriguez@gmail.com (O. Rodríguez-Leor).
@oriolrodriguez5

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Diferencias regionales en la atención al IAMCEST en España. Datos del Registro de Código Infarto ACI-SEC

RESUMEN

Introducción y objetivos: Las diferencias geográficas y organizativas entre distintas comunidades autónomas (CCAA) pueden generar diferencias en la atención al infarto agudo de miocardio con elevación del segmento ST (IAMCEST). Se han comparado 17 programas de Código Infarto en términos de incidencia, características clínicas, tratamiento de reperfusión, retraso hasta la reperfusión y mortalidad a 30 días.
Métodos: Estudio observacional prospectivo nacional (83 centros en 17 redes de infarto). El periodo de selección fue de 3 meses (1 de abril a 30 de junio de 2019), con seguimiento clínico a 30 días.
Resultados: Se incluyeron 4.366 pacientes con IAMCEST. La tasa de incidencia fue variable entre las CCAA ($p < 0,0001$), igual que el sexo ($p = 0,003$) y la prevalencia de factores de riesgo cardiovascular ($p < 0,0001$). El tratamiento de reperfusión fue angioplastia primaria (rango 77,5-97,8%), fibrinolisis (rango 0- 12,9%) o ninguno (rango 2,2-13,5%). El análisis del retraso hasta la reperfusión mostró diferencias significativas ($p < 0,001$) para todos los intervalos analizados. Hubo diferencias significativas en la mortalidad cruda a 30 días que desaparecieron tras ajustar por las características clínicas y dependientes de la red asistencial (primer contacto, tiempo hasta la reperfusión y abordaje de críticos).
Conclusiones: Se han detectado diferencias en la atención al IAMCEST entre las distintas CCAA, en términos de incidencia, características clínicas, tratamiento de reperfusión, retraso hasta la reperfusión y mortalidad a 30 días. Las diferencias en mortalidad desaparecen tras ajustar por las características del paciente y de la red asistencial.

Palabras clave: IAMCEST. Características de la población. Angioplastia.

Abbreviations

ACI-SEC: Interventional Cardiology Association at the Spanish Society of Cardiology. **AC:** autonomous communities. **pPCI:** primary percutaneous coronary intervention. **STEMI:** ST-segment elevation myocardial infarction.

INTRODUCTION

Infarction Code networks are key to treat ST-segment elevation myocardial infarction (STEMI) in the shortest time possible while optimizing reperfusion therapy.[1] In Spain we have 17 different public regional STEMI networks, 1 in each autonomous community (AC) for a total of 83 pPCI-capable hospitals in programs on a 24/7/365 basis.[2] According to data from the Annual Activity Registry of the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC), back in 2019, a total of 22 529 interventional procedures were performed in patients with infarction.[3] Recently, an analysis of the ACI-SEC Infarction Code Registry revealed the characteristics of infarction care in Spain with 87.5%, 4.4%, and 8.1% of the patients with STEMI being treated with pPCI, fibrinolysis, and without reperfusion, respectively. The 30-day mortality rate of STEMI was 7.9% dropping down to 6.8% in patients treated with pPCI.[4]

The geographical differences and heterogeneity of the organizational infrastructure among the different Infarction Code programs available can lead to regional differences as a survey conducted among health professionals involved in these programs revealed recently.[5] These organizational differences can have an impact on the management of patients with STEMI. Their analysis and AC-based comparison facilitates finding matters where there is room for improvement to optimize treatment.

This analysis compared the incidence rate, clinical characteristics, type and time to reperfusion, the characteristics of pPCI, and the 30-day mortality rate of 17 different regional programs of the Infarction Code in Spain.

METHODS

Study design

The Registry design has already been introduced[4]. In conclusion, this was a national, observational, and prospective study of 83 centers from 17 different regional STEMI networks. The patients' recruitment period was 3 months—from April 1 through June 30, 2019—with a 30-day clinical follow-up.

Registry protocol was approved by the reference central ethics committee that did not deem the obtention of the informed consent necessary since data anonymity was guaranteed at any time.

Inclusion criteria

All consecutive patients who, during the study period, triggered the activation of different regional infarction care networks with a final diagnosis of STEMI and met the following criteria were included in the study: *a)* diagnosis of ST-segment elevation acute coronary syndrome with symptoms consistent with acute coronary syndrome, electrocardiogram showing ST-segment elevation or new-onset left bundle branch block or suspected posterior infarction of, at least, 24-hour evolution since symptom onset or *b)* recovered cardiac arrest with suspected coronary etiology or *c)* cardiogenic shock with suspected coronary etiology.

Definition and collection of variables

Clinical variables were registered in an online form and previously published.[4] The definitions of the different time intervals since

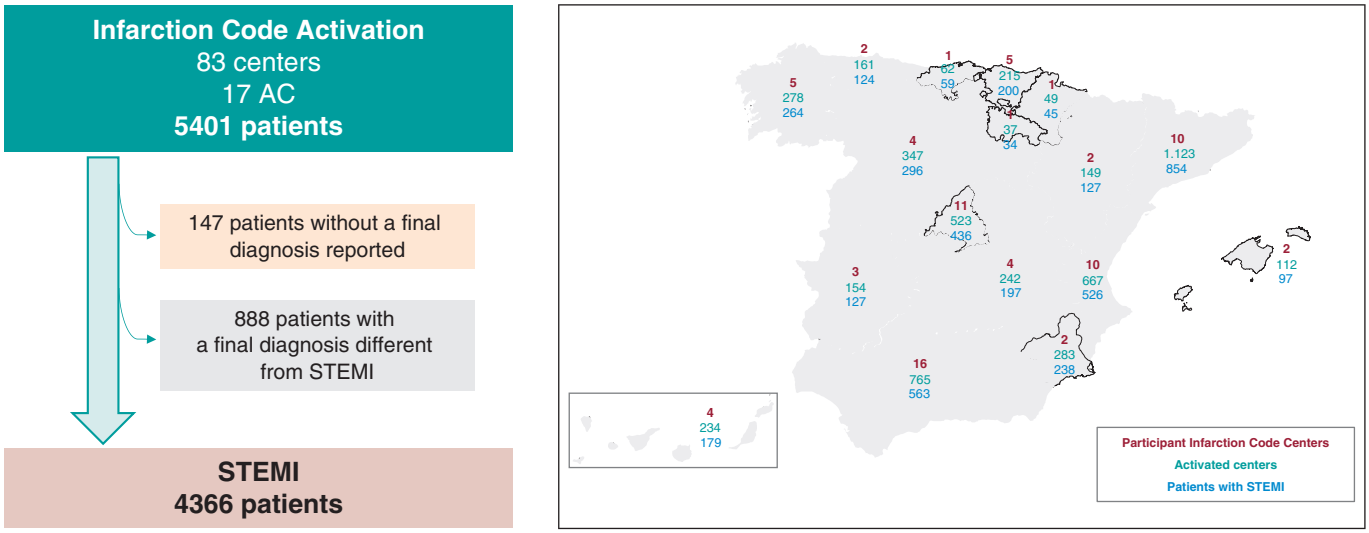


Figure 1. Flow of patients and distribution across the different autonomous communities (AC) based on participant centers, number of codes activated, and number of patients with ST-segment elevation myocardial infarction (STEMI) as final diagnosis.

symptom onset until reperfusion were given based on the recommendations established by the European clinical practice guidelines on the management of STEMI.[1] Subjective judgment from a local investigator was requested on the delay sustained by the patient since his first medical contact (existence of unjustified delay—yes/no—and reason why). To estimate the incidence rate (number of cases per million inhabitants) population data from the National Statistics Institute from 2019 were used.[6] Regarding the mortality adjusted analysis, the following characteristics of the care network were defined: the individual responsible for the first medical contact (emergency medical services, health center, non-pPCI-capable hospital, pPCI-capable hospital), time to reperfusion, and location where critical care was administered (intensive care unit or cardiac surgery intensive care unit).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. The categorical ones were expressed as frequencies and percentages. Inter-group comparisons of baseline variables were conducted using the chi-square test or the Student *t* test, when appropriate. Times to reperfusion were expressed as median and interquartile range and compared using the Mann-Whitney *U* test.

Poisson regression coefficient was used to estimate the 30-day mortality rate of each AC including patient-dependent factors (the confounding factors included were age, sex, hypertension, diabetes, dyslipidemia, smoking, previous ischemic heart disease, Killip classification, and anterior location of STEMI), and the healthcare network involved (location of the first medical contact, time between the onset of pain and reperfusion, and location where critically ill patients were treated).

The variable AC was introduced in the model in a second step, and a test of ratio of verisimilitude was performed to verify its statistical significance. When the AC variable was added, adjusted associations were obtained between AC and mortality. The Poisson regression coefficients became incidence rates using the marginal effect function. The estimated 30-day mortality rate for each AC was obtained from a mean distribution of confounding factors, which facilitated comparing mortality rate across the different AC. This method had been previously used in the acute myocardial infarction setting.[7-9] Since there could be a selection bias across the different AC in patients without reperfusion therapy, these were not included in the adjusted mortality analysis.

P values < .05 were considered statistically significant. The STATA statistical software package version 15 SE (Stata Corp, College Station, United States) was used.

RESULTS

Patients

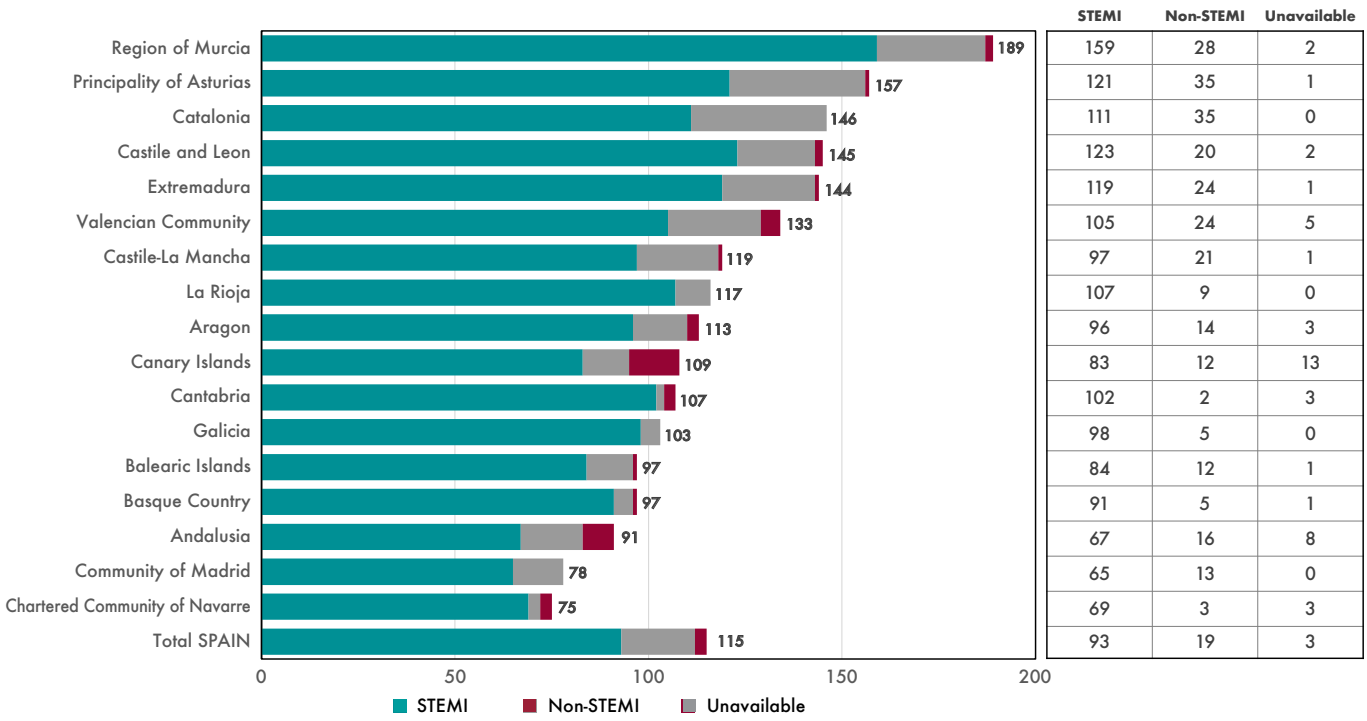
The registry included a total of 5401 patients, 4366 (81.2%) of whom had a final diagnosis of STEMI. The 888 patients (16.4%) with a diagnosis different from STEMI and the 147 (2.7%) without a final diagnosis were excluded from the analysis. Figure 1 shows the flow of patients and the AC-based distribution. Figure 2 shows the number of patients treated across the different AC plus the final diagnosis achieved adjusted by million inhabitants.[6] Table 1 shows the clinical characteristics of patients with STEMI across the different AC.

Reperfusion therapy used in patients with ST-segment elevation myocardial infarction

Out of the 4366 patients with STEMI, 3792 (86.9%) received pPCI, 189 (4.3%) fibrinolysis, and 353 (8.1%) no reperfusion therapy whatsoever. No reperfusion therapy was reported in 32 patients (0.7%). Figure 3 shows treatment distribution based on AC. Table 2 shows, across different AC and patients treated with cardiac catheterization, the angiographic findings and characteristics of interventional therapy had this procedure been performed.

Time intervals between symptom onset and reperfusion in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

Table 3 shows time intervals between symptom onset and reperfusion. Figure 4 shows the different time intervals analyzed for every AC with significant differences in all of them. Figure 5 summarizes



	STEMI	Non-STEMI	Unavailable
Region of Murcia	159	28	2
Principality of Asturias	121	35	1
Catalonia	111	35	0
Castile and Leon	123	20	2
Extremadura	119	24	1
Valencian Community	105	24	5
Castile-La Mancha	97	21	1
La Rioja	107	9	0
Aragon	96	14	3
Canary Islands	83	12	13
Cantabria	102	2	3
Galicia	98	5	0
Balearic Islands	84	12	1
Basque Country	91	5	1
Andalusia	67	16	8
Community of Madrid	65	13	0
Chartered Community of Navarre	69	3	3
Total SPAIN	93	19	3

Figure 2. Patients treated across the different autonomous communities (AC) adjusted for million inhabitants. AC were arranged from largest to smallest number of patients treated per million inhabitants. Regarding the population estimate per million inhabitants, population data from the National Statistics Institute were used.[6] STEMI, ST-segment elevation myocardial infarction.

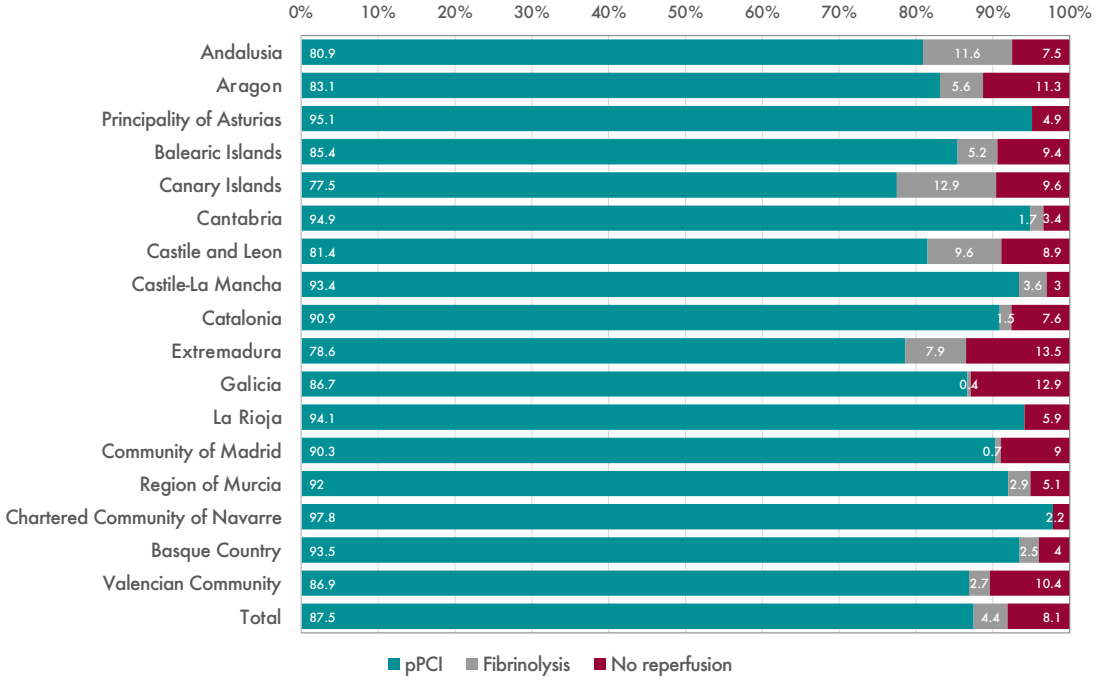


Figure 3. Distribution of reperfusion therapy in patients with ST-segment elevation myocardial infarction by autonomous communities. pPCI, primary percutaneous coronary intervention.

Table 1. Clinical characteristics of patients with ST-segment elevation myocardial infarction treated in the Infarction Code networks per autonomous community

	Age, years	Sex, women	AHT	Diabetes	Dyslipidemia	Active smoking	Previous IHD	Previous PCI	Previous stroke	Early Killip I	Early Killip IV	Anterior location
Andalusia	63 ± 13	110/563 (19.5)	297/560 (53.0)	159/558 (28.5)	252/559 (45.1)	264/557 (47.4)	60/561 (10.7)	59/559 (10.6)	31/556 (5.6)	423/541 (78.2)	31/541 (5.7)	223/521 (42.8)
Aragon	65 ± 14	30/127 (23.6)	62/127 (48.8)	28/125 (22.4)	56/127 (44.1)	59/124 (47.6)	13/124 (10.5)	17/126 (13.5)	7/122 (5.7)	99/124 (79.8)	13/124 (10.5)	56/120 (46.7)
Principality of Asturias	66 ± 13	40/124 (32.3)	61/124 (49.2)	34/122 (27.9)	54/124 (43.6)	41/123 (33.3)	20/123 (16.3)	19/123 (15.4)	7/123 (5.6)	96/123 (78.1)	11/123 (8.9)	57/122 (46.7)
Balearic Islands	63 ± 12	28/97 (28.9)	44/94 (46.8)	21/94 (22.3)	49/93 (52.7)	49/93 (52.7)	14/93 (15.1)	14/94 (14.9)	4/92 (4.4)	71/96 (74.0)	5/96 (5.2)	30/92 (32.6)
Canary Islands	60 ± 12	40/178 (22.5)	99/178 (55.6)	52/178 (29.2)	102/177 (57.6)	93/178 (52.3)	22/178 (12.4)	18/178 (10.1)	8/176 (4.6)	146/168 (86.9)	14/168 (8.3)	65/163 (39.9)
Cantabria	62 ± 13	15/59 (25.4)	31/59 (52.5)	21/58 (36.2)	27/58 (46.6)	31/57 (54.4)	10/58 (17.2)	10/59 (17.0)	3/57 (5.3)	46/56 (83.9)	2/56 (3.6)	25/58 (43.1)
Castile and Leon	64 ± 13	56/296 (18.9)	146/293 (49.8)	73/291 (25.1)	126/292 (43.2)	117/292 (40.1)	31/293 (10.6)	31/294 (10.5)	12/176 (4.1)	236/287 (82.2)	17/287 (5.9)	138/280 (49.3)
Castile-La Mancha	64 ± 13	26/197 (13.2)	108/194 (55.7)	58/192 (30.2)	99/196 (50.5)	92/193 (47.7)	19/192 (9.9)	18/194 (9.3)	9/194 (4.6)	157/196 (80.1)	12/196 (6.1)	89/194 (45.9)
Catalonia	63 ± 13	195/854 (22.8)	393/854 (46.0)	198/854 (23.2)	340/854 (39.8)	354/854 (41.4)	60/854 (7.0)	62/854 (7.3)	30/854 (3.5)	683/826 (82.7)	67/826 (8.1)	351/767 (45.8)
Extremadura	63 ± 13	18/127 (14.2)	74/127 (58.3)	26/126 (20.6)	52/126 (41.3)	48/127 (37.8)	17/126 (13.5)	14/126 (11.1)	4/127 (3.2)	91/122 (74.6)	11/122 (9.0)	56/121 (46.3)
Galicia	63 ± 13	63/264 (23.9)	130/262 (49.6)	48/259 (18.5)	138/261 (52.9)	100/215 (46.5)	18/261 (6.9)	25/262 (9.5)	12/263 (4.6)	195/251 (77.7)	31/251 (12.4)	103/233 (44.2)
La Rioja	59 ± 12	8/34 (23.5)	14/34 (41.2)	3/34 (8.8)	16/34 (46.1)	20/34 (58.8)	1/34 (3.0)	2/34 (5.9)	0/34 (0)	30/34 (88.2)	3/34 (8.8)	11/34 (32.4)
Community of Madrid	63 ± 13	105/436 (24.1)	212/432 (49.1)	88/430 (20.5)	208/431 (48.3)	177/428 (41.4)	41/429 (9.6)	43/429 (10.0)	11/429 (2.6)	347/424 (81.8)	35/424 (8.3)	174/419 (41.5)
Region of Murcia	64 ± 13	43/238 (18.1)	127/237 (53.6)	71/237 (30.0)	100/237 (42.4)	110/237 (46.4)	41/237 (17.3)	24/151 (15.9)	3/151 (2.0)	196/237 (82.7)	18/237 (7.6)	101/231 (43.7)
Chartered Community of Navarre	65 ± 14	14/45 (31.1)	18/44 (40.9)	9/45 (20.0)	29/45 (64.4)	16/45 (35.6)	3/45 (6.7)	4/44 (9.1)	3/45 (6.7)	31/43 (72.1)	4/43 (9.3)	16/44 (36.4)
Basque Country	64 ± 14	52/200 (26.0)	101/197 (51.3)	39/197 (19.8)	101/198 (51.0)	89/197 (45.2)	26/195 (13.3)	32/196 (16.3)	11/193 (5.7)	169/200 (84.5)	12/200 (6.0)	83/199 (41.7)
Valencian Community	63 ± 13	119/526 (22.6)	293/519 (56.5)	163/514 (31.7)	212/514 (41.3)	235/514 (45.7)	56/515 (10.9)	53/511 (10.4)	21/513 (4.1)	445/520 (85.6)	34/520 (6.5)	217/503 (43.1)
P	.054	.003	.038	< .0001	< .0001	.007	< .0001	.011	.61	.016	.25	.44
Total	63 ± 13	962/4365 (22.0)	2210/4335 (51.0)	1091/4314 (25.3)	1961/4326 (45.3)	1895/4268 (44.4)	452/4318 (10.5)	445/4234 (10.5)	176/4222 (4.2)	3462/4248 (81.5)	320/4248 (7.5)	1795/4101 (43.8)

AHT, arterial hypertension; IHD, ischemic heart disease; PCI, percutaneous coronary intervention.
Data are expressed as no. (%) or mean ± standard deviation.

the causes of unjustified delays between the first medical contact and reperfusion for every AC.

Mortality analysis in patients with ST-segment elevation myocardial infarction

Table 4 includes unadjusted mortality data at hospital admission and 30 days, and mortality for the adjusted model.

30-day mortality rate was different across different AC ($P < .001$). When the analysis was adjusted for patient-dependent factors and the healthcare network, mortality difference across the AC lost its statistical significance ($P = .19$).

DISCUSSION

This study is a comparative of how the different STEMI care programs work in Spain. Results show differences in the incidence rate, the patients' clinical profile, revascularization therapy, the characteristics of the interventional procedure performed, infarction care times, and the 30-day unadjusted mortality rate. Although mortality differences

Table 2. Angiographic findings and characteristics of interventional procedures in patients with ST-segment elevation myocardial infarction treated with cardiac catheterization per autonomous community

	Radial access	No. of diseased vessels	Early TIMI grade-0/1 flow	Final TIMI grade-3 flow	Need for hemodynamic support	Thrombus aspiration in IRA	BMS implantation in IRA	DES implantation in IRA	pPCI	Bailout PCI	Elective PCI after fibrinolysis	Coronary angiography without PCI
Andalusia	456/534 (85.4)	1.49 ± 0.69	416/535 (77.8)	502/536 (93.7)	15/563 (2.7)	76/563 (13.5)	48/563 (8.5)	456/563 (81.0)	471/557 (84.6)	36/557 (6.5)	27/557 (4.9)	23/557 (4.1)
Aragon	111/122 (91.0)	1.62 ± 0.78	90/120 (75.0)	114/122 (93.4)	5/127 (3.9)	41/127 (32.3)	0/127 (0)	103/127 (81.1)	108/124 (87.1)	6/124 (4.8)	1/124 (0.8)	9/124 (7.3)
Principality of Asturias	99/121 (81.8)	1.54 ± 0.77	106/121 (87.6)	111/121 (91.7)	5/124 (4.0)	39/124 (31.5)	10/124 (8.1)	98/124 (79.0)	118/123 (95.9)	0/123 (0)	0/123 (0)	5/123 (4.1)
Balearic Islands	79/92 (85.9)	1.46 ± 0.67	67/92 (72.8)	85/92 (92.4)	0/124 (0)	27/97 (27.8)	4/97 (4.1)	80/97 (82.5)	89/96 (92.7)	4/96 (4.2)	0/96 (0)	3/96 (3.1)
Canary Islands	138/169 (81.7)	1.54 ± 0.76	131/170 (77.1)	155/169 (91.7)	6/179 (3.6)	29/179 (16.2)	3/179 (1.7)	150/179 (83.8)	145/176 (82.4)	6/176 (3.4)	15/176 (8.5)	10/176 (5.7)
Cantabria	17/56 (30.4)	1.50 ± 0.68	51/57 (89.5)	55/56 (98.2)	1/59 (1.7)	31/59 (52.5)	0/59 (0)	51/59 (86.4)	57/59 (96.6)	0/59 (0)	1/59 (1.7)	1/59 (1.7)
Castile and Leon	263/281 (93.6)	1.55 ± 0.74	192/241 (79.7)	225/247 (91.1)	15/296 (5.1)	27/296 (9.1)	9/296 (3.0)	249/296 (84.1)	255/291 (96.6)	12/291 (4.1)	16/291 (5.5)	8/291 (2.8)
Castile-La Mancha	164/191 (85.9)	1.68 ± 0.73	164/192 (85.4)	186/190 (97.9)	9/197 (4.6)	75/197 (38.1)	10/197 (5.1)	172/197 (97.3)	185/196 (94.4)	2/196 (1.0)	4/196 (2.0)	5/196 (2.6)
Catalonia	727/781 (93.1)	1.48 ± 0.70	594/844 (70.4)	787/827 (95.2)	ND	259/854 (30.3)	117/854 (13.7)	653/854 (76.5)	807/849 (95.1)	8/849 (0.9)	3/849 (0.4)	31/849 (3.7)
Extremadura	119/121 (98.4)	1.65 ± 0.79	104/122 (85.3)	104/122 (85.3)	6/127 (4.7)	18/127 (14.2)	12/127 (11.0)	98/127 (77.2)	112/126 (88.9)	8/126 (6.4)	2/126 (1.6)	4/126 (3.2)
Galicia	228/242 (94.2)	1.53 ± 0.84	182/229 (79.5)	214/229 (93.5)	20/264 (7.6)	77/264 (29.2)	4/264 (1.5)	215/264 (81.4)	246/264 (93.2)	0/264 (0)	0/264 (0)	18/264 (6.8)
La Rioja	29/34 (85.3)	1.15 ± 0.36	30/34 (88.2)	31/34 (91.2)	0/24 (0)	10/34 (29.4)	3/34 (8.8)	27/34 (79.4)	33/34 (97.1)	0/34 (0)	0/34 (0)	1/34 (2.9)
Community of Madrid	395/421 (93.8)	1.48 ± 0.69	329/402 (81.8)	392/425 (92.2)	23/436 (5.3)	80/436 (18.4)	15/436 (3.4)	352/436 (80.5)	421/434 (97.0)	3/434 (0.7)	0/434 (0)	10/434 (2.3)
Region of Murcia	213/237 (89.9)	1.48 ± 0.64	175/234 (74.8)	223/236 (94.5)	4/238 (1.7)	56/238 (23.5)	5/238 (2.1)	209/238 (87.2)	226/238 (95.0)	7/238 (2.9)	0/238 (0)	5/238 (2.1)
Chartered Community of Navarre	31/36 (86.1)	2.00 ± 0.86	34/43 (79.1)	39/45 (86.7)	6/45 (13.3)	22/45 (48.9)	2/45 (4.4)	39/45 (86.7)	44/45 (97.8)	0/45 (0)	0/45 (0)	1/45 (2.2)
Basque Country	179/198 (90.4)	1.51 ± 0.67	153/198 (77.3)	191/199 (96.0)	7/200 (3.5)	100/200 (50.0)	3/200 (1.5)	174/200 (87.0)	194/199 (97.5)	4/199 (2.0)	1/199 (0.5)	0/199 (0)
Valencian Community	484/514 (94.2)	1.59 ± 0.76	390/496 (78.6)	461/497 (92.8)	8/256 (1.5)	145/526 (27.6)	34/526 (6.5)	423/526 (80.4)	482/518 (93.1)	10/518 (1.9)	4/518 (0.8)	22/518 (4.3)
P	< .0001	.84	< .0001	.002	< .0001	< .0001	< .0001	.004	< .0001			
Total	3732/4150 (89.9)	1.50 ± 0.71	3208/4130 (77.7)	3875/4147 (93.4)	110/4366 (2.5)	1112/4366 (25.5)	281/4366 (6.4)	3548/4366 (81.3)	3992/4329 (92.2)	106/4329 (2.5)	74/4329 (1.7)	157/4329 (3.6)

BMS, bare metal stent; CL, cath lab; DES, drug-eluting stent; ECG, electrocardiogram; EMS, emergency medical services; FMC, first medical contact; IRA, infarct-related artery; PCI, percutaneous coronary intervention; pPCI, primary percutaneous coronary intervention.
The type of procedure performed (pPCI, bailout angioplasty, elective PCI after fibrinolysis or coronary angiography without PCI) is on the total number of patients treated with coronary angiography, not on the total number of patients with ST-segment elevation myocardial infarction.
Data are expressed as no. (%).

reduce, they're still significantly different after adjusting for the patients' risk and clinical characteristics. Also, they disappear after adjusting for whoever is responsible for the first medical contact, time to reperfusion, and location where critical care is administered, all of them factors associated with the way each network is organized.

Both functioning and results of infarction care networks are highly influenced by different factors like geography, the number of capable centers, transfer times, the availability of the right resources, infrastructure, and the characteristics of each healthcare system.[2] In Spain, the plan of each AC has been designed independently. Also, the services rendered by the different AC is not homogeneous since resource allocation by the different administrations of the 17 Spanish AC is decentralized[2] in such a way that there are inequalities in the ways these networks are organized.[2,5,10,11] A recent consensus document on the requirements and sustainability of pPCI programs in

Table 3. Location of the first medical contact and time intervals between the first medical contact and reperfusion per autonomous community

	First EMS care	First care provided at the health center	First non-pPCI-capable center care	First pPCI-capable center care	Transfer without going to the CL right away*	Time of onset of pain to FMC	Time of FMC to ECG	Time of FMC to pPCI-capable center in transferred patients	Time from FMC to reperfusion	Time from onset of pain to reperfusion
Andalusia	206/537 (38.4)	138/537 (25.7)	93/537 (17.3)	100/537 (18.6)	188/427 (44.0)	60 [30-123]	5 [3-10]	80 [50-120]	113 [70-170]	195 [135-330]
Aragon	46/123 (37.4)	23/123 (18.7)	42/123 (34.1)	12/123 (9.8)	23/110 (20.9)	62.5 [18.5-170]	7 [4-12.5]	84.5 [45-145]	116.5 [70.5-177.5]	229 [126-345]
Principality of Asturias	32/123 (26.0)	18/123 (14.6)	36/123 (29.3)	37/123 (30.1)	4/86 (4.7)	80 [32-210]	10 [5-22]	85 [60-119]	108 [73-137]	215 [134.5-351]
Balearic Islands	33/95 (34.7)	26/95 (27.4)	27/95 (28.4)	9/95 (9.5)	3/85 (3.5)	70 [30-164]	6 [5-10]	100 [55-139]	124 [85-169]	197.5 [143.5-391]
Canary Islands	28/178 (15.7)	103/178 (57.9)	22/178 (12.4)	25/178 (14.0)	77/152 (50.7)	75 [37.5-150]	9 [5-15]	85 [55-133]	122 [95-172]	220 [159-385]
Cantabria	15/58 (25.9)	19/58 (32.8)	13/58 (22.4)	11/58 (19.0)	26/46 (56.5)	53 [25-145]	5 [4.5-10]	60 [35-93]	110 [81-188]	210 [134-303.5]
Castile and Leon	97/290 (33.5)	70/290 (27.2)	68/290 (23.5)	46/290 (15.9)	70/237 (29.5)	90 [35-221]	8 [4-15]	115 [70-165]	135 [85-197]	242.5 [163-432.5]
Castile-La Mancha	69/196 (35.2)	61/196 (31.1)	30/196 (17.3)	36/196 (18.4)	49/160 (30.6)	68 [30-160]	10 [5-15]	86.5 [58-114]	109 [80-155]	205 [150-322]
Catalonia	332/847 (39.2)	161/847 (19.0)	256/847 (30.2)	98/847 (11.6)	115/730 (15.8)	63 [30-160]	6 [3-14]	75 [55-105]	104 [80-138]	180 [127-288]
Extremadura	43/126 (34.1)	36/126 (28.6)	22/126 (17.5)	25/126 (19.8)	27/93 (29.0)	81.5 [44-135]	10 [5-12]	91.5 [60-143]	121 [90-178]	240 [160-360]
Galicia	84/264 (31.8)	111/264 (42.1)	28/264 (10.6)	41/264 (15.5)	ND	60 [26-179]	9 [5-19]	95 [70-140]	115 [88.5-163]	194 [134-353]
La Rioja	10/34 (29.4)	9/34 (26.5)	6/34 (17.7)	9/34 (26.5)	3/25 (12.0)	76.5 [35-110]	4.5 [1-10]	70 [46-86]	90.5 [67-114]	159.5 [118.5-212.5]
Community of Madrid	196/429 (45.7)	37/429 (8.6)	80/429 (18.7)	116/429 (27.0)	142/309 (45.6)	63 [35-140]	6 [3-12]	60 [42-85]	95 [75-130]	178.5 [135-257.5]
Region of Murcia	102/238 (42.9)	36/238 (15.1)	74/238 (31.1)	26/238 (10.9)	25/212 (11.8)	56.5 [24-131]	5 [5-10]	80 [60-120]	103 [79-160]	175 [130-305]
Chartered Community of Navarre	22/45 (48.9)	7/45 (15.6)	3/45 (6.7)	13/45 (28.9)	12/32 (37.5)	63.5 [29.5-124.5]	1 [0-5]	50 [35-91]	90 [69-140]	175 [128-262]
Basque Country	76/199 (38.2)	28/199 (14.1)	37/199 (18.6)	58/199 (29.2)	61/138 (44.2)	80 [32-184]	6.5 [3-11]	61 [49-77]	97 [75-135]	210 [134-345]
Valencian Community	128/521 (24.6)	146/521 (28.0)	128/521 (24.6)	119/521 (22.8)	98/398 (24.6)	82 [35-180]	5 [0-10]	94 [65-135]	120 [93-165]	220 [146-348]
P	< .0001	< .0001	< .0001	< .0001	< .001	.001	.0001	.0001	.0001	.0001
Total	1519/4303 (35.3)	1038/4303 (24.1)	965/4303 (22.4)	781/4303 (18.2)	923/3240 (28.5)	67 [30-165]	7 [4-15]	80 [55-120]	110 [80-154]	197 [135-330]

CL, cath lab; ECG, electrocardiogram; EMS, emergency medical services; FMC, first medical contact; pPCI, primary percutaneous coronary intervention.
* Patients treated early in a non-pPCI-capable center requiring immediate transfer to a pPCI-capable center.
Data are expressed as no. (%) or mean [interquartile range]. Times are expressed in minutes.

Spain proposed measures to homogenize and secure their sustainability.[2,12] Our study data reinforce the need for taking measures like the proposals made in the said consensus document.

Differences in the patients' clinical profile

Registry data demonstrated a difference in the number of codes activated per million inhabitants. Also, in the number of patients with STEMI per million inhabitants across the different AC. These differences are multifactorial and can be seen, historically, in the ACI-SEC annual activity registry reports.[3] Some AC have older populations and more cardiovascular risk factors, which could account for the higher rate of infarction reported.[6] However, the lack of a unified criterion on the indication for Infarction Code activation could also account for these differences seen.[5]

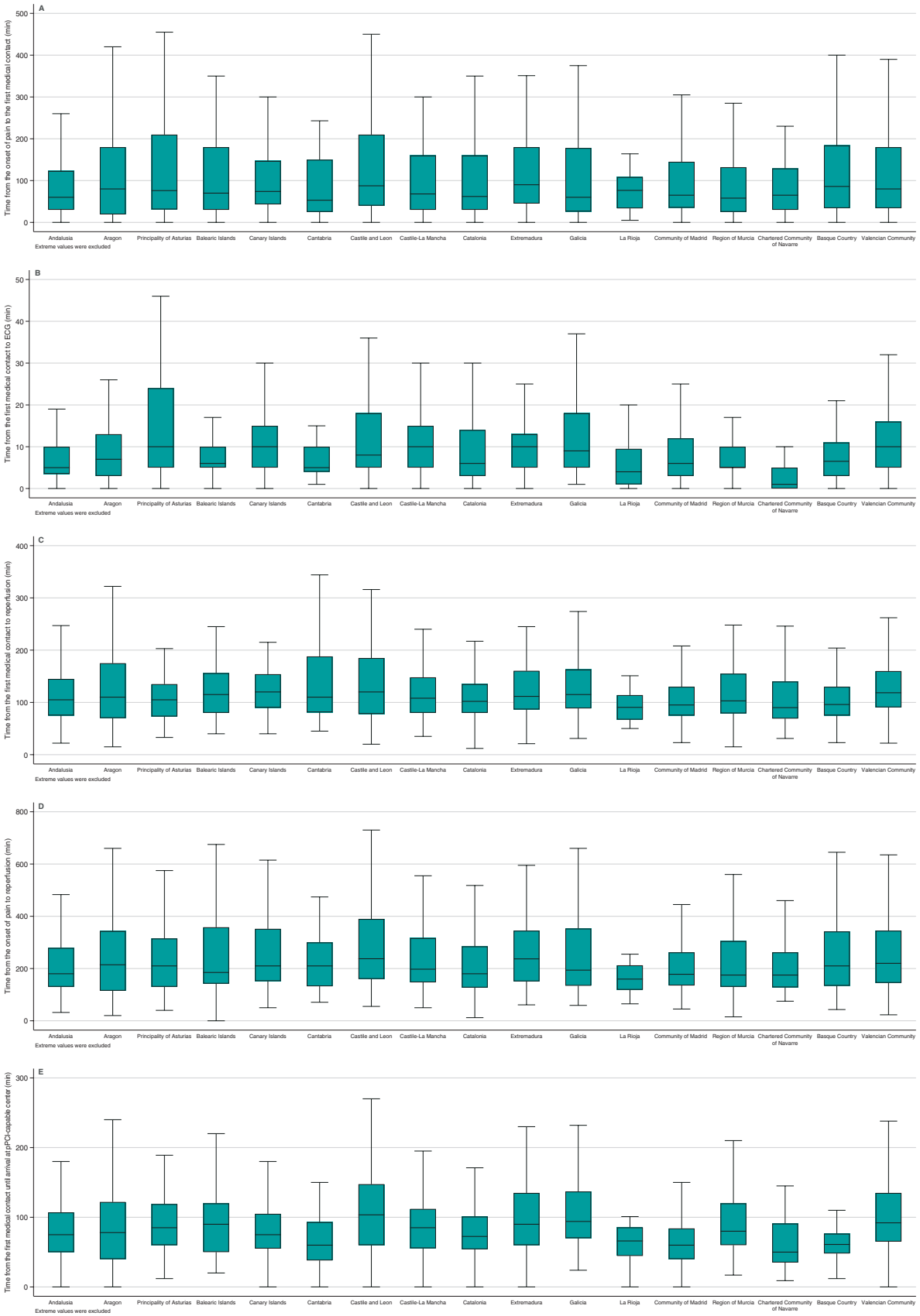


Figure 4. Time intervals between symptom onset and reperfusion in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention (pPCI) for every autonomous community. **A:** time in min from the onset of pain to the first medical contact. **B:** time in min from the first medical contact to the electrocardiogram (ECG). **C:** time in min from the first medical contact to reperfusion. **D:** time in min from the onset of pain to reperfusion. **E:** time in min from the first medical contact to the arrival at the pPCI-capable center in patients requiring transfer from a non-pPCI-capable center.

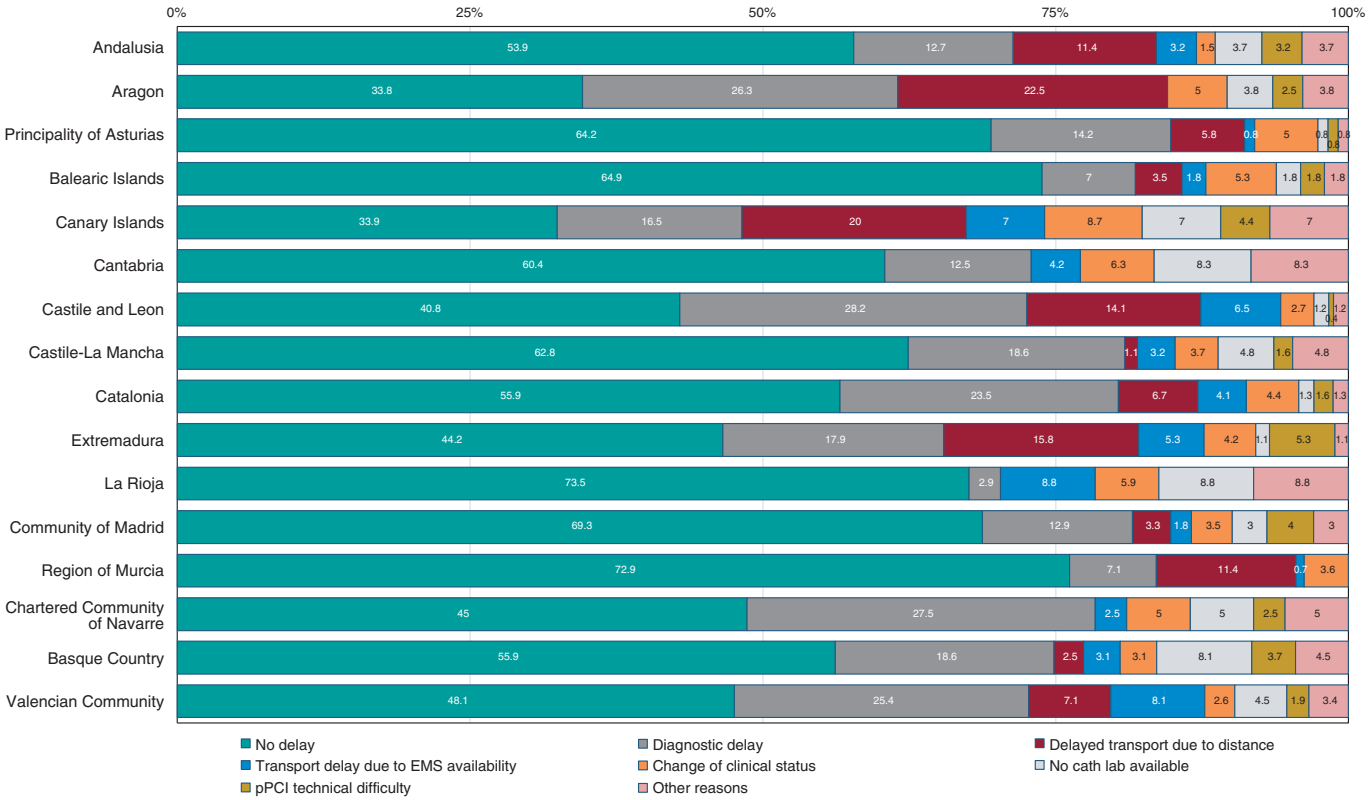


Figure 5. Causes of unjustified time delays between the first medical contact and reperfusion. Unjustified time delays did not imply, necessarily, that the time between the first medical contact and reperfusion was > 120 min. As a matter of fact, overall, in 53.2% of the cases the time between the first medical contact and reperfusion was < 120 min, and, among these, excessive time delays were reported in 21.5%. EMS, emergency medical services; pPCI, primary percutaneous coronary intervention.

Differences in reperfusion therapy

pPCI is the treatment of choice for the management of STEMI.[1] The geographical (populations far from pPCI-capable centers) and organizational characteristics (availability of medical service transport with ECG monitorization) across the different AC lead to a variable number of patients be treated with fibrinolysis. A previous analysis of data on the *Codi Infart* in Catalonia revealed that patients treated with fibrinolysis in non- pPCI-capable centers had worse disease progression compared to those transferred to pPCI-capable centers within the first 140 min after diagnosis.[13]

Different time delays to reperfusion

Patient-dependent time delays (from symptom onset to first medical contact) were highly variable. Although the geographic distribution of the population could partially account for these differences, public campaigns should be run to increase awareness on STEMI symptoms and the need for calling out-of-hospital emergency care.[1]

System-dependent time delays (from first medical contact to reperfusion) is much easier to change with organizational measures. Also, it determines prognosis.[14] Time delays to reperfusion depend on whoever is involved in the first medical contact. Therefore, patients treated by emergency medical services—those with the shortest times—showed high variability across the different programs. Better access to these systems for the population would also improve time delays to reperfusion.[15]

European clinical practice guidelines on the management of STEMI describe quality indicators that should be observed by the infarction networks to reduce the time to reperfusion, among these, a single coordination centralized center, interpreting the ECG before arriving at the hospital to achieve diagnosis and activate the system early, the direct transfer of patients to the cath lab without ER or ICU admissions or the follow-up of infarction care times, among other.[1] Our study demonstrated that not all programs meet these recommendations meaning that, in many cases, there is a huge room for improvement. For example, currently, it does not seem reasonable that a significant number of patients who need to be transferred to the pPCI (up to 50% in some cases) wouldn't end up at the cath lab right away. This simple measure can reduce time to reperfusion in 20 min and have a direct impact on prognosis.[16,17]

The presence of unjustified delayed reperfusion times was highly variable across the different AC, as well as the causes for these delays, which is indicative of the characteristics of each AC.

Mortality differences

A study conducted by Cequier et al.[18] analyzed standardized mortality based on the risk of patients with STEMI across different AC from 2003 through 2012 and detected significant differences. However, across this period, not all regions had implemented Infarction Code programs and the rate of pPCI was highly variable. Our study demonstrated that there are still differences in crude mortality that disappear after adjusting for the clinical variables and care network-related variables (location of first medical contact, delay to reperfusion, and management of critically ill patients). We have already mentioned the importance that the first medical contact should be performed by emergency medical services and

Table 4. Mortality analysis in patients treated with primary percutaneous coronary intervention per autonomous community

	Unadjusted hospital mortality	Unadjusted 30-day mortality	Adjusted 30-day mortality
Andalusia	30/563 (5.3)	37/523 (7.1)	6.0 [5.3-6-7]
Aragon	8/127 (6.3)	8/124 (6.5)	5.5 [4.0-6.9]
Principality of Asturias	9/124 (7.3)	10/118 (8.5)	6.7 [5.4-8.0]
Balearic Islands	6/97 (6.2)	6/88 (6.8)	5.0 [3.3-6.7]
Canary Islands	15/179 (8.4)	15/155 (9.7)	7.0 [5.5-8.6]
Cantabria	0/59 (0)	0/59 (0)	0
Castile and Leon	18/296 (6.1)	23/270 (8.5)	8.4 [7.1-9.8]
Castile-La Mancha	9/197 (4.6)	10/191 (5.2)	3.1 [2.3-3.8]
Catalonia	29/854 (3.4)	58/801 (7.2)	6.0 [5.4-6.6]
Extremadura	12/127 (9.5)	16/125 (12.8)	8.1 [6.6-9.5]
Galicia	22/264 (8.3)	28/260 (10.8)	6.8 [5.6-7.9]
La Rioja	1/34 (2.9)	1/33 (3.0)	5.6 [2.3-8.9]
Community of Madrid	14/436 (3.2)	21/421 (5.0)	3.9 [3.3-4.6]
Region of Murcia	21/237 (8.9)	24/226 (10.6)	9.2 [8.0-10.5]
Chartered Community of Navarre	5/45 (11.1)	5/45 (11.1)	9.5 [6.7-12.3]
Basque Country	12/200 (6.0)	16/197 (8.1)	8.9 [7.4-10.4]
Valencian Community	47/526 (8.9)	55/499 (11.0)	10.2 [9.2-11.2]
P	< .001	< .001	.19
Total	258/4365 (5.9)	337/4166 (8.1)	–

Data are expressed as no. (%) or mean [interquartile range].

the measures used to reduce time to reperfusion. Regarding the management of critically ill patients, a study conducted by Sánchez-Salado et al.[19] of 20 000 patients with cardiogenic shock demonstrated that the availability of cardiac surgery intensive care units was associated with a lower mortality rate. Data from this study added to the finding of our registry support the need for expanding the availability of cardiac surgery intensive care units in large volume centers of patients with acute coronary syndrome. In conclusion, the results of mortality study suggest that the organization of the different networks would increase the crude mortality rate seen in some AC.

Limitations

This study has some limitations. In the first place, it is based on self-reported data without external auditing. However, data on interventional cardiology are rather standardized across the world, and the electronic form for data curation was designed to be applied both intuitively and universally. Also, data from Catalonia and Galicia were collected from their official registries, reviewed, and then audited.

Secondly, the profile of patients may have been different across the different AC. To address this limitation and its possible impact on the different crude mortality rates reported, a mortality study was conducted across different AC after adjusting for different clinical variables and care networks. Therefore, some models may be over-adjusted, which is why formal statistical comparisons across AC should be interpreted as cautious as the associations described in any observational trial. The model did not include patients lacking some of the variables included in the model. Table 1 of the supplementary data shows patients discarded from the study for every AC.

Thirdly, patients with STEMI treated outside the infarction networks were not included in this study, although this is probably indicative of a mild selection bias due to its reduced number. Therefore, the greater bias occurs in patients without reperfusion therapy, who, at times, are not covered by these networks. For this reason, these patients were not considered in the mortality analysis. Similarly, patients with myocardial infarction and subacute presentation without emergency reperfusion criteria were not included in the study.

Fourthly, the way of collecting times may have presented some differences between centers and AC. However, since this was a prospective study with previously established definitions, we believe that these differences may have been minimized.

In the fifth place, the data presented date back to 2019. Since then, no big organizational changes have occurred to justify changes in the dynamics of functioning or relevant changes have been made in the European guidelines on the management of STEMI (published back in 2017). Also, in a study conducted during the first wave of the COVID-19 pandemic no differences were seen regarding the type of reperfusion therapy used or time between the first medical contact and reperfusion. However, an increased mortality rate was seen attributed, among other causes, to longer ischemia times.[20]

Finally, this study only included patients for a period of 3 months. However, we think these data can be generalized to what happens in a much larger period.

CONCLUSIONS

This registry showed significant differences in STEMI care across the different Spanish AC regarding incidence rate, the patients' clinical characteristics, reperfusion therapy, time delays to reperfusion, and 30-day crude mortality rate. After adjusting for the clinical characteristics and variables associated with the care network, no differences mortality differences were reported across the different AC.

Standardizing the organization and functioning of Infarction Code networks could correct some of the differences seen in the management of STEMI.

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AUTHORS' CONTRIBUTIONS

Drafting of the manuscript: O. Rodríguez-Leor, A.B. Cid-Álvarez, A. Pérez de Prado, and X Rosselló. Process of manuscript revision: all the authors. Statistical analysis: O. Rodríguez-Leor, and X. Rosselló. Database review: O. Rodríguez-Leor, A.B. Cid-Álvarez, and A. Pérez de Prado. Data coordination across the different regional network: all the authors.

CONFLICTS OF INTEREST

A. Pérez de Prado received numerous personal fees from iVascular, Boston Scientific, Terumo, Bbraun, and Abbott Vascular. Á. Cequier received personal fees from Ferrer International, Terumo, Astra Zeneca, and Biotronik. R. Moreno, S. Ojeda, R. Romaguera, and A. Pérez de Prado are associate editors of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The remaining authors did not declare any conflicts of interest associated with the content of this manuscript.

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SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000360.

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