molecular bases in pulmonary arterial hypertension (PI 18/01233). The CNIC is supported by the *Instituto de Salud Carlos III* (ISCIII), the Ministry of Science and Innovation and the Pro CNIC Foundation, and is a Severo Ochoa Center of Excellence (SEV-2015-0505).

Jorge Nuche,[a,b,c,d] Carmen Pérez-Olivares,[b]
Teresa Segura de la Cal,[b] Carmen Jiménez López-Guarch,[a,b,d]
Fernando Arribas Ynsaurriaga,[a,b,d] and Pilar Escribano Subías[a,b,d,*]

[a]*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[b]*Servicio de Cardiología, Hospital Universitario 12 de Octubre, Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain*
[c]*Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain*
[d]*Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain*

* Corresponding author:
E-mail address: pilar.escribano.subias@gmail.com
(P. Escribano Subías).

Available online 30 May 2020

REFERENCES

1. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. *JAMA Cardiol.* 2020. http://dx.doi.org/10.1001/jamacardio.2020.1286.
2. Harder EM, Small AM, Fares WH. Primary cardiac hospitalizations in pulmonary arterial hypertension: Trends and outcomes from 2001 to 2014. *Respir Med.* 2020;161:105850.
3. Hemnes AR, Rathinasabapathy A, Austin EA, et al. A potential therapeutic role for angiotensin-converting enzyme 2 in human pulmonary arterial hypertension. *Eur Respir J.* 2018;51:1702638.
4. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med.* 2005;11:875–879.
5. Araz O. Current Pharmacological Approach to ARDS: The Place of Bosentan. *Eurasian J Med.* 2020;52:81–85.
6. Marini JJ, Gattinoni L. Management of COVID-19 Respiratory Distress. *JAMA.* 2020. http://dx.doi.org/10.1001/jama.2020.6825.

Decrease in ST-segment elevation myocardial infarction admissions in Catalonia during the COVID-19 pandemic

Reducción de los ingresos por infarto agudo de miocardio con elevación del segmento ST en Cataluña durante la pandemia de COVID-19

To the Editor,

On February 2020, the coronavirus disease of 2019 (COVID-19) rapidly spread throughout Europe. Due to the lack of pharmacological treatment or vaccine, governments adopted measures called social distancing to reduce the peak intensity of the epidemic. In Spain, the government issued a decree declaring a state of alarm on 14 March, 2020.

Timely reperfusion therapy by primary percutaneous coronary intervention (pPCI) is recommended for patients with ST-segment elevation myocardial infarction (STEMI)[1] and its benefit is time-dependent, with longer delays associated with worse outcomes. A recent survey of Spanish STEMI networks reported a reduction in pPCI procedures during the COVID-19 pandemic.[2] We aimed to assess the reduction in STEMI admissions and changes in patient characteristics, delay times and early mortality during the first weeks of the COVID-19 pandemic in Catalonia.

In Catalonia, a Spanish region with 7.6 million inhabitants, acute care for patients with STEMI is organized through a regional network of 10 pPCI hospitals.

The AMI code registry collects data from all attended STEMI patients. The registry belongs to the health department of the Catalan government and its completion is compulsory and periodically audited. The database conforms to ethical and legal requirements for research purposes, and all study procedures are conducted in accordance with the ethical standards of the Helsinki Declaration.

All patients with a confirmed STEMI from 1 March to 19 April, 2020, were compared with patients attended within the same dates in 2019.

Delay times were defined according to the European Guidelines.[1] Patient delay was defined as time from symptom onset to first medical contact. System delay as time from first contact to reperfusion therapy. Ischemia time as time from symptom onset to reperfusion therapy. Delay times were stratified by site of first medical contact.

Admission rates were estimated with Poisson regression models with time (days) as a continuous variable. Categorical variables are expressed as number and percentage and were compared with the chi-square test. Continuous variables are expressed as mean ± standard deviation and were compared with the Student *t* test. Time intervals are expressed as median [interquartile range] and were compared with the Kruskal-Wallis equality-of-populations rank test. Mortality at 10 days after activation was estimated for all patients with available information about vital status (STEMI occurring between March 1 and April 10).

A total of 395 STEMI patients were admitted during the 2020 period and 524 during the same period in 2019. The mean number of daily admissions was 10.5 in 2019 and 7.9 in 2020 (incidence rate ratio, 0.75; 95% confidence interval, 0.66-0.86). In 2020, there was a significant 52% reduction in daily admissions from day 1 to day 50 (figure 1). There were few differences between the groups (table 1).

A similar reduction in STEMI admissions has already been reported in other settings.[3–5] To our knowledge, this is the first study performed in Spain using individual patient data from a regional STEMI network. We observed a 50% reduction in STEMI admissions in 50 days and only slight differences in patient characteristics and delay times compared with patients admitted during the same period in 2019. Potential causes of this decrease in STEMI admissions include avoidance of medical care due to social distancing, STEMI underdiagnosis, and competing risk
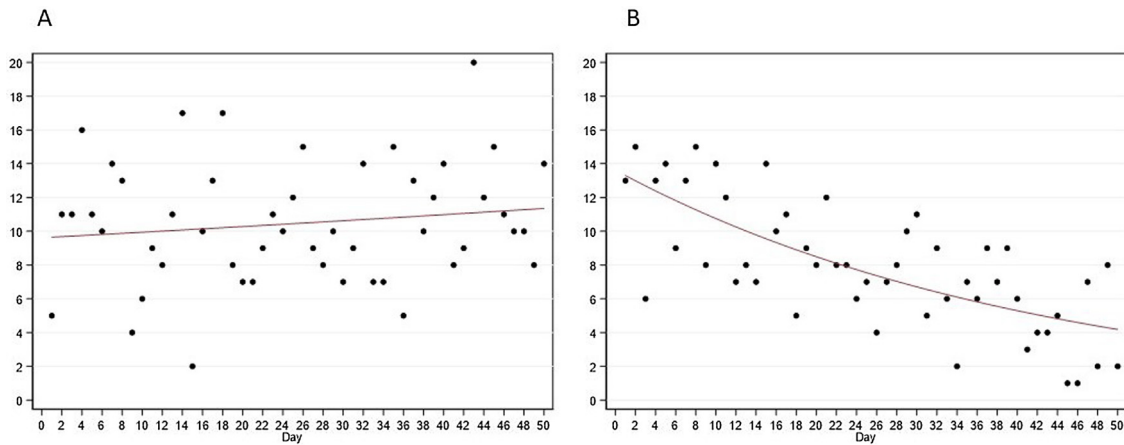
Figure 1. Daily rate of confirmed ST-segment elevation myocardial infarction admissions between March 1 and April 19 in 2019 (A) and 2020 (B).

Table 1
Characteristics, delay times and outcomes of patients with confirmed ST-segment elevation acute myocardial infarction

	Valid n	2019	Valid n	2020	P
Female sex	524	109 (20.8)	395	78 (19.8)	.694
Age	524	63.4 ± 0.6	395	61.9 ± 0.7	.104
Age > 80 y	524	70 (13.4)	395	37 (9.4)	.062
Previous history of cardiovascular disease	524	73 (13.9)	395	64 (16.2)	.339
First assisted in hospital	524	232 (44.3)	395	145 (36.7)	.021
Sudden cardiac death	524	33 (6.3)	395	18 (4.6)	.254
Killip III-IV	501	53 (10.6)	387	43 (11.1)	.800
pPCI	519	425 (81.1)	394	337 (85.3)	.141
TIMI flow pre (no flow)	311	195 (62.7)	296	195 (65.9)	.414
TIMI flow post (normal)	309	298 (96.4)	292	279 (96)	.577
Delay time, median [q25-q75]					
Patient delay					
Attended by EMS	174	49 [24-90]	156	59 [29-132.5]	.059
Attended at hospitals	302	115 [45-280]	212	105 [52-284]	.898
System delay					
Attended by EMS	141	80 [65-98]	133	83 [65-99]	.526
Attended at hospitals	266	94 [71-131]	196	103.5 [80.5-133]	.051
Total ischemia time					
Attended by EMS	140	141 [115-193]	134	160.5 [125-231]	.095
Attended at hospital	265	239.5 [150-434]	192	239.5 [155–424]	.790
Door-to-balloon time	309	20 [15-27]	295	22 [18-29]	.041
10-day mortality	385	22 (5.7)	340	24 (7.1)	.459

EMS, emergency medical system; pPCI, primary percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.
Data are expressed as No. (%), mean ± standard deviation or median [interquartile range].

with the acquisition and severity of COVID-19, and warrant further investigation.

Rafael Romaguera,[a,b] Aida Ribera,[b,c,d,*] Francesc Güell-Viaplana,[e] Carlos Tomás-Querol,[f] Juan Francisco Muñoz-Camacho,[g] and Víctor Agudelo[h] on behalf of the Codi IAM investigators

[a]*Servicio de Cardiología, Hospital Universitario de Bellvitge – IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain*
[b]*Departamento de Salud, Plan Director de Enfermedades*

Cardiovasculares, Generalitat de Catalunya, Barcelona, Spain
^c*Unidad de Epidemiología Cardiovascular, Servicio de Cardiología, Hospital Universitario Vall d'Hebron – Institut de Recerca Vall d'Hebron (VHIR), Barcelona, Spain*
^d*Centro de Investigación Biomédica en Red Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain*
^e*Área Asistencial, Servei Català de la Salut, Generalitat de Catalunya, Barcelona, Spain*
^f*Servicio de Cardiología, Hospital Universitario Arnau de Vilanova – IRBLleida, Lleida, Spain*
^g*Servicio de Cardiología, Hospital Universitario Mutua de Terrassa, Terrassa, Barcelona, Spain*
^h*Servicio de Cardiología, Hospital Universitario de Girona Josep Trueta, Girona, Spain*

* Corresponding author:
E-mail address: aida.ribera@vhir.org (A. Ribera).

Available online 5 June 2020

REFERENCES

1. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J.* 2018. https://doi.org/10.1093/eurheartj/ehx393
2. Rodríguez-Leor O, Cid-Álvarez B, Ojeda S, et al. Impact of the COVID-19 pandemic on interventional cardiology activity in Spain. *REC Interv Cardiol.* 2020;2:82–89.
3. Tam CCF, Cheung KS, Lam S, et al. Impact of Coronavirus Disease 2019 (COVID-19) Outbreak on ST-Segment-Elevation Myocardial Infarction Care in Hong Kong. *China Circ Cardiovasc Qual Outcomes.* 2020. https://doi.org/10.1161/CIRCOUTCOMES.120.006631
4. De Filippo O, D'Ascenzo F, Angelini F, et al. Reduced Rate of Hospital Admissions for ACS during Covid-19 Outbreak in Northern Italy. *N Engl J Med.* 2020. https://doi.org/10.1056/NEJMc2009166
5. Garcia S, Albaghdadi MS, Meraj PM, et al. Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States during COVID-19 Pandemic. *J Am Coll Cardiol.* 2020. https://doi.org/10.1016/j.jacc.2020.04.011

Identification by next-generation sequencing of 2 novel cases of noncompaction cardiomyopathy associated with 1p36 deletions

Identificación mediante secuenciación de nueva generación de dos nuevos casos de miocardiopatía no compactada asociada a deleciones 1p36

To the Editor,

Left ventricular noncompaction (LVNC) is a structural abnormality characterized by a thin compacted epicardial layer and a thick endocardial layer with prominent trabeculations and deep recesses. When associated with cardiomyopathy, a genetic cause may be identified. Mutations in several genes, including tafazzin (*TAZ*), α-dystrobrevin (*DTNA*), Z-band alternatively spliced PDZ-motif protein (*ZASP*), lamin A/C (*LMNA*) and genes encoding sarcomeric proteins, have been reported.[1] However, the yield of genetic testing appears to be relatively low, with clinically relevant variants identified in approximately 40% of cases. Frequently, limited information on the genes involved make it difficult to classify the variants identified.[2] Most studies did not test for the presence of copy number variations (CNVs). CNVs, defined as gains or losses of DNA, contribute to the development of multiple genetic disorders and can be responsible for complex traits. In particular, 1p36 deletion has been associated with the development of LVNC cardiomyopathy in the context of a complex phenotype.[3] Arndt et al.[3] suggested that cardiac manifestations would likely depend on the involvement of the *PRDM16* gene. Next-generation sequencing (NGS) coverage-based CNV analysis provides accurate tools for detecting CNVs. For this reason, the *PRDM16* gene was included in our inherited cardiovascular diseases panels, and we systematically test our patients for CNVs in this gene. We identified 2 *PRDM16* deletions in 382 patients referred with clinical suspicion of LVNC cardiomyopathy. No deletion affecting this gene was identified in more than 12 000 patients submitted with other cardiovascular phenotypes.

Patient 1 was a 25-year-old woman with LVNC cardiomyopathy (figure 1A) and complex phenotype diagnosed at 6 months old with mild facial dysmorphism, cognitive impairment, and epileptic encephalopathy. Sensorineural hearing loss was ruled out. Cardiac magnetic resonance imaging could not be performed due to claustrophobia and Holter monitoring showed no arrhythmias. Her parents and brother were unaffected. NGS coverage-based CNV analysis identified a heterozygous deletion of the *PRDM16* gene. Single nucleotide polymorphism (SNP) array confirmed the deletion of a region comprising 112 genes, including *PRDM16* (figure 1B). The deletion was confirmed to be *de novo* (figure 1C) and considered pathogenic.

Patient 2 was a 23-year-old man evaluated after the sudden death of his father at age 43. In this case, autopsy was not performed. Echocardiogram showed LVNC without systolic impairment (figure 2A). Cardiac magnetic resonance imaging showed no late gadolinium enhancement and no arrhythmias were detected during Holter monitoring. No extracardiac anomalies were observed. NGS coverage-based CNV analysis identified a heterozygous deletion of *PRDM16* exons 2 to 17 in the proband and also confirmed this deletion in his 20-year-old sister. She had LVNC and mild systolic dysfunction (figure 2B). SNP array in the proband confirmed a deletion of 11 genes, including *PRDM16* (figure 2C). The deletion was absent in the unaffected mother (figure 2D) and considered likely pathogenic. However, the presence of the mutation could not be tested on the paternal side.

Heterozygous 1p36 deletion is the most common subtelomeric deletion syndrome. It is believed to affect between 1 in 5000 and 1 in 10 000 newborns, although these may be underestimates. The associated phenotype is characterized by psychomotor retardation, hearing deficits, seizures, dysmorphic facial features, noncompaction/dilated cardiomyopathy, intellectual disability, and other congenital anomalies.[4] There is high clinical variability among individuals, which could be explained by variation in the length of the deletions or the genes involved. Some of these genes have been individually associated with heart defects and/or developmental abnormalities.[5] Arndt et al.[3] used *in situ* hybridization to identify a common deletion region among patients with 1p36 deletion syndrome who presented with cardiomyopathy. This region included only the terminal 14 exons of *PRDM16*. These authors also found pathogenic variants in a proportion of nonsyndromic LVNC and dilated cardiomyopathy. Other chromosomal abnormalities (eg, 1q43