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

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Valid n</th>
<th>2019</th>
<th>Valid n</th>
<th>2020</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>524</td>
<td>109 (20.8)</td>
<td>395</td>
<td>78 (19.8)</td>
<td>.694</td>
</tr>
<tr>
<td>Age (years)</td>
<td>524</td>
<td>63.4 ± 0.6</td>
<td>395</td>
<td>61.9 ± 0.7</td>
<td>.104</td>
</tr>
<tr>
<td>Age ≥ 80 y</td>
<td>524</td>
<td>70 (13.4)</td>
<td>395</td>
<td>37 (9.4)</td>
<td>.062</td>
</tr>
<tr>
<td>Previous history of cardiovascular disease</td>
<td>524</td>
<td>73 (13.9)</td>
<td>395</td>
<td>64 (16.2)</td>
<td>.339</td>
</tr>
<tr>
<td>First assisted in hospital</td>
<td>524</td>
<td>232 (44.3)</td>
<td>395</td>
<td>145 (36.7)</td>
<td>.021</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>524</td>
<td>33 (6.3)</td>
<td>395</td>
<td>18 (4.6)</td>
<td>.254</td>
</tr>
<tr>
<td>Killip III–IV</td>
<td>501</td>
<td>53 (10.6)</td>
<td>387</td>
<td>43 (11.1)</td>
<td>.800</td>
</tr>
<tr>
<td>pPCI</td>
<td>519</td>
<td>425 (81.1)</td>
<td>394</td>
<td>337 (85.3)</td>
<td>.141</td>
</tr>
<tr>
<td>TIMI flow pre (no flow)</td>
<td>311</td>
<td>195 (62.7)</td>
<td>296</td>
<td>195 (65.9)</td>
<td>.414</td>
</tr>
<tr>
<td>TIMI flow post (normal)</td>
<td>309</td>
<td>298 (96.4)</td>
<td>292</td>
<td>279 (96)</td>
<td>.577</td>
</tr>
</tbody>
</table>

Delay time, median [q25–q75]

Patient delay


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 [119-193] | 134 | 160.5 [125-231] | .095 |
| Attended at hospitals | 265 | 239.5 [150-434] | 192 | 239.5 [155-424] | .790 |

Door-to-balloon time

| 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].

Figure 1. Daily rate of confirmed ST-segment elevation myocardial infarction admissions between March 1 and April 19 in 2019 (A) and 2020 (B).
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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 delecciones 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.4 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.5 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.6 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

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