

# Gender differences in mortality in patients with ST-segment elevation myocardial infarction

## Diferencias de género en la mortalidad en pacientes con infarto de miocardio con elevación del segmento ST

Grecia I.M. Raymundo-Martínez<sup>1\*</sup>, Diego Araiza-Garaygordobi<sup>2</sup>, Rodrigo Gopar-Nieto<sup>1</sup>, Arnoldo E. Loáisiga-Sáenz<sup>1</sup>, Luis A. Baeza-Herrera<sup>1</sup>, Ricardo Pohls-Vázquez<sup>1</sup>, Laura V. Torres-Araujo<sup>1</sup>, Manuel Martínez-Ramos Méndez<sup>1</sup>, Arturo I. Alonso<sup>3</sup>, Itzel V. Delgado-Cruz<sup>3</sup>, Diestefano E. Ronquillo-Ramírez<sup>3</sup>, and Alexandra Arias-Mendoza<sup>2</sup>

<sup>1</sup>Cardiology Fellow, National Institute of Cardiology Ignacio Chávez, Mexico City, Mexico; <sup>2</sup>Department of Coronary Care Unit and Emergency, National Institute of Cardiology Ignacio Chávez, Mexico City, Mexico; <sup>3</sup>Research fellow. National Institute of Cardiology Ignacio Chávez, Mexico City, Mexico

### Abstract

**Objective:** Women with ST-segment elevation myocardial infarction (STEMI) have worst outcomes than men. The objective of the study was to determine gender differences in mortality in patients with STEMI. **Methods:** Cohort study including patients with STEMI. We recorded demographic and clinical data, laboratory tests, and in-hospital mortality in patients who underwent primary angioplasty and pharmacoinvasive strategy. Kaplan–Meier analysis was used to assess mortality differences between both genders. **Results:** A total of 340 patients were analyzed, 296 males and 44 females. Mean age of the female group was  $64.3 \pm 12.3$  years. About 98% of females were among Killip-Kimball Class I-II. They had higher risk scores compared to man, longer ischemic time and first medical contact with a difference in comparison to man of 47 and 60 min, respectively. Mortality was 9.1% (4) in the female group. **Conclusions:** Although the proportion of women had higher mortality than man, we did not find any difference with statistical significance probably due to the lack of representation. We need more awareness in the female population about STEMI, since longer first medical contact time and longer total ischemic time might be one possible explanation of a higher mortality.

**Key words:** Myocardial infarction. Gender difference. ST-segment elevation myocardial infarction. Mortality.

### Resumen

**Objetivo:** Las mujeres con infarto agudo al miocardio con elevación del segmento ST (SICA CEST) tienen peor pronóstico que los hombres. El objetivo fue determinar las diferencias de mortalidad en género en pacientes con SICA CEST. **Metodos:** Estudio de cohorte de pacientes con SICA CEST. Se recolectaron datos demográficos, clínicos, de laboratorio y mortalidad intrahospitalaria. Se realizó un análisis de Kaplan-Meier para valorar la mortalidad y determinar diferencias de género. **Resultados:** Se analizaron 340 pacientes, 296 hombres y 44 mujeres. Se observó que las mujeres tuvieron mayores puntajes en los scores de riesgo, mayor tiempo de primer contacto y tiempo total de isquemia encontrando una diferencia con el grupo de hombres de 47 y 60 minutos respectivamente. La mortalidad intrahospitalaria fue de 9.1% (4) sin diferencia estadísticamente significativa en comparación con los hombres. **Conclusiones:** Aunque la proporción de mujeres tuvo mayor mortalidad no se encontró

### Correspondence:

\*Grecia I.M. Raymundo-Martínez  
E-mail: graymundo87@gmail.com

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*diferencia estadísticamente significativa en comparación con los hombres probablemente por el tamaño de la muestra debido a baja representación del grupo femenino. Se necesita mayor conciencia en relación al infarto en el grupo de mujeres, ya que mayor tiempo de primer contacto y mayor tiempo total de isquemia pueden ser una posible explicación de una mayor mortalidad.*

**Palabras clave:** Infarto agudo al miocardio. Diferencia de género. SICA CEST. Mortalidad.

## Introduction

Ischemic heart disease represents the primary cause of death in Mexico<sup>1-5</sup>, mostly attributed to acute myocardial infarction. Women have been underrepresented in most trials regarding ischemic heart disease and it is well known that women have risk factors of their own, which makes it questionable to say that treatment tested is as effective in this group, because differences in survival and mortality have been significantly different through the years. Globally, coronary artery disease has been more prevalent in women than in men. Around the world, the mean age of presentation of myocardial infarction in women is 64.5 years of age, and it carries a worst prognosis. Those who have a first event before the age of 50 double the risk of mortality compared to men<sup>1-3,6-10</sup>. Bowles et al. acknowledged that women in his study did not attribute cardiovascular symptoms to ST-segment elevation myocardial infarction (STEMI), but to extracardiac causes<sup>10</sup>. As we know, timely reperfusion for STEMI carries better outcomes. Pharmacoinvasive strategy (PS) has proven in several clinical trials to be as effective as primary percutaneous coronary intervention (PPCI) especially when is implemented in places where demographic and socioeconomic represent an issue when it comes to perform PPCI. Even though PS is equally effective than PPCI, women keep having higher mortality rates. The national program for the reduction of mortality in STEMI carried out by health department and by the National Heart Institute in Mexico, revealed that 8 out of every 19 patients did not have information regarding STEMI, and only one-third of females had a correct identification of symptoms. Interviewed women had less knowledge or wrong concept of STEMI. Most women did acknowledge that they would search for medical attention if having an event, but this does not correlate to the real world because the first medical contact for women tends to be higher than men<sup>11</sup>. There is a high percentage of death in women than in men, being consistently higher in every age group, even when the cases are more frequent in men<sup>11</sup>. For this reason, the aim of this study was to determine the differences in gender and outcomes in patients with STEMI in the Mexican

population who were taken either to PS or PPCI within the PHASE-MX registry<sup>12</sup>.

## Methods

A cohort from the PHASE-MX trial was taken, which included patients with both genders, between 18 and 80 years of age, with a diagnosis of STEMI, that were admitted in the Emergency Department and Coronary Care Unit of the National Heart Institute Ignacio Chavez from April 1 of 2018 to March 31 of 2019. The area of care and reference of the Mexico City metropolitan area comprise a calculated area of 7954 km<sup>2</sup>, with a population of 20.4 million inhabitants. Patients from 60 hospitals from the metropolitan area were received. At admission, the following data were collected: age, gender, date of admission, the presence of diabetes mellitus, systemic arterial hypertension, smoking, chronic kidney disease, obesity, previous history of myocardial infarction, previous revascularization, vital signs, TIMI, GRACE and CRUSADE scores, blood biometrics, blood glucose, troponin, NT proBNP, total ischemic time, first medical contact time, door-to-needle time, door-to-wire crossing or device time, medical treatment before reperfusion, time to PS, and treatment success. In-hospital follow and date of home discharge were registered.

## Statistical analysis

STATA v13 (StataCorp LP, College Station, Tx) was used. Quantitative variables were analyzed with descriptive methods depending on their normality, corroborated by the Shapiro–Wilk test. Parametric variables were described with mean value and standard deviation. In the case of non-parametric variables, median and interquartile ranges were used. Likewise, taking into consideration, the normality of each quantitative variable, an analysis with Student's t-test and Mann–Whitney U-test was performed. Qualitative variables were described through frequencies and percentages, while for the bivariate analysis, the  $\chi^2$  or the Fisher's test was performed depending on the number of events. Cox regression models were built to find association

**Table 1.** Demographic characteristics in patients with STEMI and comparison of those taken to PS versus PCI

Variable	Total (n = 340)		PS (n = 166)		PCI (n = 174)		p
	n	%	n	%	n	%	
Male	296	87.1	148	89.2	148	85.1	0.26
Female	44	12.9	18	10.8	26	14.9	
Diabetes mellitus	119	35	58	34.9	61	35.1	0.98
Systemic arterial hypertension	159	46.8	72	43.4	87	50	0.22
Dyslipidemia	58	17.1	21	12.7	37	21.3	0.03
Current smoking	157	46.2	88	53	69	39.7	0.01
Ceased smoking	56	16.5	23	13.9	33	18.97	0.2
Chronic kidney disease	7	2.1	4	2.4	3	1.72	0.47
Obesity	77	22.7	35	21.1	42	24.1	0.50
Previous myocardial infarction	33	9.7	14	8.4	19	10.9	0.43
Previous PCI	23	6.8	7	4.3	16	9.2	0.05
Previous CABG	5	1.5	1	0.6	4	2.3	0.20
Heart failure	3	0.9	0	0	3	1.7	0.08
Valvular heart disease	2	0.6	0	0	2	1.2	0.26
Atrial fibrillation	1	0.3	0	0	1	0.6	0.32
	<b>n</b>	<b>Mean ± SD</b>	<b>n</b>	<b>Mean ± SD</b>	<b>n</b>	<b>Mean ± SD</b>	<b>p</b>
Age (years)	340	59 ± 10.8	166	58.5 ± 10.9		60 ± 11	0.08

PS: pharmacoinvasive strategy; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; SD: standard deviation. STEMI: ST-segment elevation myocardial infarction.

between risk factors and mortality (dependent variable) in patients treated with both strategies. For the survival analysis, tables and Kaplan–Meier curves were made to describe mortality in both groups.  $p < 0.05$  was considered as statistically significant.

## Results

A total of 340 patients were analyzed, 296 males and 44 females (Table 1). Mean age of the female group was  $64.3 \pm 12.3$  years. Among the female group, 56.8% had diabetes mellitus, 50.1% had systemic arterial hypertension, 5.9% had dyslipidemia, 18.2% actively smoking, 2.3% had chronic kidney disease, 15.9% had obesity, 11.4% had previous myocardial infarction, 9.7% had previous percutaneous coronary intervention, 2.3% had previous coronary artery bypass graft, 2.3% had some sort of valvular heart disease, and 2.3% had heart failure. There were no cases with atrial fibrillation (Table 2).

At arrival, 98% of females were among Killip-Kimball Class I-II. The mean heart rate was 77 bpm, mean respiratory rate was 18 bpm, mean systolic arterial pressure was 116 mmHg, mean diastolic arterial pressure was 71.5 mmHg, and mean pulse oximetry was 92%. As far as clinical risk scores, mean TIMI score was 5 points, mean GRACE score was 146.5 points, and mean CRUSADE score was 39.5 points with statistically significant difference compared to men (Table 3).

Within the laboratory evaluation at arrival in the women's group, the mean hemoglobin was 14.2 g/dl, mean creatinine was 0.84 g/dl, mean urea nitrogen was 19.2 mg/dl, mean leukocytes was  $10.7 \times 10^3 \mu\text{L}$ , and NT proBNP value was significantly higher than men, 1750 versus 688 ( $p = 0.00$ ), respectively. Initial and maximal troponin levels did not show statistical difference compared to men. Mean serum glucose in the women's group was 193.5 mg/dl being significantly higher than men whom mean value was 156 mg/dl ( $p = 0.01$ ), and this was reflected in the glycated

**Table 2.** Demographic data at arrival of patients with STEMI

Variable	Total (n = 340)		Male (n = 296)		Female (n = 44)		p
	n	%	n	%	n	%	
Diabetes mellitus	119	35	94	31.8	25	56.8	0.00*
Systemic arterial hypertension	159	46.8	133	44.9	26	59.1	0.07*
Dyslipidemia	58	17.1	51	17.2	7	15.9	0.82*
Current smoking	157	46.2	149	50.3	8	18.2	0.00*
Ceased smoking	56	16.5	50	16.9	6	13.6	0.58*
Chronic kidney disease	7	2.1	6	2	1	2.3	0.62*
Obesity	77	22.7	70	23.7	7	15.9	0.25*
Previous myocardial infarction	33	9.7	28	9.5	5	11.4	0.69*
Previous PCI	23	6.8	19	6.4	4	9.1	0.34*
Previous CABG	5	1.5	4	1.4	1	2.3	0.50*
Heart failure	3	0.9	2	0.7	1	2.3	0.29*
Valvular heart disease	2	0.6	1	0.3	1	2.3	0.24*
Atrial fibrillation	1	0.3	1	0.3	0	0	0.69*
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	p
Age (years)	340	59 ± 10.8	296	58.3 ± 10.4	44	64.3 ± 12.3	0.00+

PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; SD: standard deviation. \*Chi squared, +Student's t-test (independent). STEMI: ST-segment elevation myocardial infarction.

**Table 3.** Vital signs and risk scores at admission in patients with STEMI

Variable	Total (n = 340)		Male (n = 296)		Female (n = 44)		p
	n	%	n	%	n	%	
Killip-Kimball I	181	54.4	160	55.4	21	47.7	0.36*
Killip-Kimball II	132	39.6	111	38.4	21	47.7	
Killip-Kimball III	10	3	8	2.8	2	4.6	
Killip-Kimball IV	10	3	10	3.5	0	0	
	n	Median (IQR)	N	Median (IQR)	n	Median (IQR)	p
Heart rate (bpm)	340	75.5 (68.5-90)	296	75 (67-90)	44	77 (70-92.5)	0.66
Respiratory rate (rpm)	340	18 (16-19)	296	18 (16-19)	44	18 (16-19.5)	0.70
Systolic arterial pressure (mmHg)	340	127 (114-147)	296	130 (117-146)	44	116 (106-157)	0.07
Diastolic arterial pressure (mmHg)	340	80 (70-90)	296	80 (70-90)	44	71.5 (64.5-82.5)	0.01
Pulse oximetry (%)	340	92 (90-95)	296	92 (90-95)	44	92 (90-94)	0.58
TIMI score	340	4 (2-5)	296	3 (2-5)	44	5 (3-7)	0.00
GRACE score	340	125 (101-150)	296	123 (100-147)	44	146.5 (110-164.5)	0.02
CRUSADE score	340	26 (18-35)	296	25 (18-33)	44	39.5 (27.5-55)	0.00

IQR: interquartile range. \*Chi cuadrado. STEMI: ST-segment elevation myocardial infarction.

**Table 4.** Laboratory findings in patients with STEMI

Variable	Total (n = 340) Median (IQR)	Male (n = 296) Median (IQR)	Female (n = 44) Median (IQR)	p
Hemoglobin (g/L)	15.6 (14.4-16.7)	15.8 (14.6-16.8)	14.2 (12.9-15.5)	0.00
Creatinine (mg/dL)	1 (0.8-1.2)	1 (0.8-1.2)	0.84 (0.7-1.1)	0.01
Urea nitrogen (mg/dL)	17 (14-23)	17 (14-22)	19.2 (14.9-32)	0.03
Sodium	136 (134-138)	136 (134-138)	135 (133-137.5)	0.44
C-reactive protein	6.9 (2.7-28.7)	6.6 (2.6-31.9)	12 (3.8-21.4)	0.38
Leukocytes	11.7 (9.3-14.4)	11.9 (9.5-14.7)	10.7 (7.9-12.9)	0.01
NT proBNP	793.5 (222.5-3284.5)	688 (194-2958)	1750 (615-4373)	0.00
Troponin I	12.7 (0.9-52.8)	12.8 (0.9-52.3)	14.1 (1.2-56.4)	0.77
Maximum troponin I	64 (24-80)	63.4 (23.9-80)	74.6 (26-80)	0.41
Serum glucose (mg/dL)	162.5 (127.8-238.5)	156 (125-230)	193.5 (140-280)	0.01
K	4.1 (3.8-4.4)	4.1 (3.8-4.4)	4.1 (3.8-4.6)	0.53
Cl	103 (100-105.52)	103 (100-105.1)	104 (100-107)	0.33
Glycated hemoglobin	6.1 (5.65-8.2)	6.1 (5.6-7.6)	7.7 (5.9-9.5)	0.00
Albumin	3.6 (3.3-3.9)	3.7 (3.4-3.9)	3.6 (3.1-3.9)	0.19
Uric acid	6.7 (5.6-7.86)	6.7 (5.6-7.9)	6.4 (5-7.1)	0.19
Platelets	217 (183-259)	214 (180-256)	241 (213-293)	0.00
Total cholesterol	154.9 (130-188.9)	154.2 (130-188.5)	167 (130-192)	0.40
LDL cholesterol	98.3 (75-121.8)	98 (75.1-121.2)	102 (74-129)	0.45
HDL cholesterol	34.4 (29.7-40)	34 (29.3-39.1)	38 (31-48)	0.00
STH	1.4 (0.7-2.8)	1.4 (0.8-2.8)	1.7 (0.9-3.6)	0.24

IQR: interquartile range; LDL: low-density lipoprotein; HDL: high-density lipoprotein; STH: stimulant thyroid hormone. STEMI: ST-segment elevation myocardial infarction.

**Table 5.** Comparison of the first medical contact time and total ischemic time in patients with STEMI

Time (min)	Total (n = 340) Median (IQR)	PS (n = 166) Median (IQR)	PCI (n = 174) Median (IQR)	p
Total ischemic time	320 (205-599)	347.5 (200-600)	310 (205-557)	0.52
First medical contact	120 (60-270)	120 (60-225)	150 (60-300)	0.11
Door-to-needle time	-	54 (30-103)	-	-
PS	-	1440 (600-2880)	-	-
Door-to-device time	-	-	72.5 (60-95)	-

PS: pharmacoinvasive strategy; PCI: percutaneous coronary intervention; SD: standard deviation; IQR: interquartile range. STEMI: ST-segment elevation myocardial infarction.

hemoglobin, mean value in females was 7.7 (5.9-9.5)%, and mean value in man was 6.1 (5.6-7.6)% ( $p = 0.00$ ) (Table 4). One hundred and sixty-six patients were taken to PS and 174 to PCI. The distribution by gender was 87.1% of male and 12.9% of female (Table 5).

Total ischemic time in the female group was 360 (214-658) min, first medical contact time was 180 (75-325) min, the door-to-needle time was 31 min (20-85), and the door-to-device time was 73 (65-93) min. In-hospital stay was similar to the male patients and the

**Table 6.** Gender difference in attention times for reperfusion, hospital stay, and LVEF in STEMI

Time	Total (n = 340)	Male (n = 296)	Female (n = 44)	p
Total ischemic time (min)	320 (205-599)	313.5 (205-589.5)	360 (214-658)	0.63
First medical contact (min)	120 (60-270)	120 (60-247.5)	180 (75-325)	0.08
Door-to-needle time (min)	54 (30-103)	60 (30-110)	31 (20-85)	0.09
Door-to-device time (min)	72.5 (60-95)	71.5 (60-96)	73 (65-93)	0.56
Hospital stay	6 (3-9)	6 (3-9)	5 (3-10)	0.68
Final LVEF	46 (39-54)	45.9 (38.5-54)	50 (40-57)	0.21

LVEF: left ventricular ejection fraction. STEMI: ST-segment elevation myocardial infarction.

**Table 7.** In-hospital mortality in patients with STEMI taken to PS versus PCI

Variable	ACP n (%)	EFI n (%)	Total n (%)
Survival	163 (93.7)	157 (94.6)	320 (94.1)
Death	11 (6.3)	9 (5.4)	20 (5.9)

p = 0.82. PS: pharmacoinvasive strategy; PCI: percutaneous coronary intervention. STEMI: ST-segment elevation myocardial infarction.

**Table 8.** Gender differences in survival

Variable	Male	Female
Survival n (%)	280 (94.6)	40 (90.9)
Mortality n (%)	16 (5.4)	4 (9.1)
Total n	296	44

p = 0.25.

left ventricular ejection fraction was 50% for the female group without differences against the male group (Table 6).

In-hospital mortality was seen in 11 patients (6.3%) who underwent PCI and 9 patients (5.4%) who underwent PS without statistical significance (Table 7). In-hospital mortality was seen in 9.1% of the female group, corresponding to 4 patients (Table 8). In the logistic regression models, factors associated with mortality in man were serum glucose > 180 mg/dl systolic arterial pressure < 90 mmHg and a GRACE score above 126 points (Table 9). In the logistic regression model for risk factors associated with mortality in the female group, there were no predictors found (Table 10).

**Table 9.** Logistic regression model for mortality in male patients with STEMI

Variable	OR	p	IC 95%
Diabetes mellitus	2.94	0.03	1.06-8.18
Hypertension	1.61	0.35	0.58-4.46
Previous myocardial infarction	3.55	0.03	1.06-11.88
Elevation of C-reactive protein	1.53	0.43	0.51-4.53
Elevation of troponin I	1.19	0.73	0.42-3.38
Elevation of serum glucose > 180 mg/dl	7.33	0.00	2.0-26.33
Total ischemic time > 180 min	2.86	0.04	1.01-8.11
Systolic arterial pressure < 90 mmHg	13.19	0.00	2.03-85.41
Diastolic arterial pressure < 60 mmHg	2.6	0.38	0.3-22.51
GRACE score > 126	4.8	0.00	1.61-14.23

OR: odds ratio. STEMI: ST-segment elevation myocardial infarction.

## Discussion

Coronary artery disease in women has had little appreciation and has been left behind due to the higher prevalence of STEMI in man before the age of 50. Our study was focused on the characterization of women who suffer STEMI, to determine demographic, clinical, and laboratory data, evaluation of attention times, and in-hospital mortality compared to man. In our study, the mean age of STEMI presentation in women is similar to other parts of the world. Furthermore, our study shows that comorbidities such as diabetes mellitus, systemic arterial hypertension, dyslipidemia, and obesity are similar to other trials. However, in comparison to men, women had higher prevalence of cigarette smoking and diabetes mellitus.

**Table 10.** Logistic regression model for mortality in female patients with STEMI

Variable	OR	p	IC (95%)
Diabetes mellitus	0.73	0.77	0.09-5.78
Hypertension	0.66	0.70	0.08-5.22
Active smoker	1.57	0.71	0.14-17.42
Elevation of C-reactive protein	0.37	0.36	0.04-3.03
Elevation of troponin I	0.6	0.62	0.07-4.71
Elevation of serum glucose > 180 mg/dl	1.79	0.62	0.17-18.91
Total ischemic time > 180 min	0.45	0.50	0.04-4.72
Systolic arterial pressure < 90 mmHg	13	0.09	0.64-263.91
Diastolic arterial pressure < 60 mmHg	4.11	0.27	0.32-52.69
GRACE score > 126	2.71	0.40	0.25-29.36

OR: odds ratio. STEMI: ST-segment elevation myocardial infarction.

These two factors might explain why women have worst prognosis than man. Nevertheless, the logistic regression model did not show any association in the overall outcome, we cannot say that there is an association to mortality. We acknowledge that this might be because of the low size sample. Therefore, it is necessary to increase the sample to show statistical significance. As we confirm a low representation of women, we also confirm the fact that not finding predictors for mortality make it difficult to implement different medical treatment for the female group. About 94% of woman had Killip-Kimball Class I-II, without differences in comparison to man. Regarding the risk score scales, women had higher TIMI, GRACE, and CRUSADE scores with statistical significance but without association to mortality. Women with ischemic heart disease have worst outcome compared to men<sup>7,8</sup>.

Those women who have a STEMI before the age to 50 are 2 times more likely to die<sup>11</sup>. Some explanations of why women die more than man are as explained by Bowles, most women do not attribute their symptoms to a cardiovascular cause which delays medical attention. This is reflected in our study since the first medical contact was much longer for women, who took 180 min to arrive to a medical facility, in comparison to man who took 120 min, meaning a delay of 60 min which again is reflected in longer total ischemic times for women, with a mean time of 360 min in comparison to man who had 313.5 min. Although we did not find a significant

statistical difference in survival between genders, the proportion of female deaths was higher than men. This might be biased by the lack of representation of the female population.

## Conclusions

Mortality in female patients who developed STEMI did not have statistical significance over men, although the proportion of female deaths was higher. They have more prevalence of diabetes mellitus, obesity, and cigarette smoking. The lack of statistical significance is probably due to the lack of representation.

The majority of women had Class Killip y Kimball I-II, have higher TIMI, GRACE, and CRUSADE scores than man, and have higher levels of NT proBNP and more serum glucose at admission than men. Most women have longer times for the first medical contact which is reflected in the higher total ischemic time.

One practical lesson for cardiologists and non cardiologists is that we should implement more registries where women are included and generate research guided by gender since the course and treatment of STEMI is different in each group. Redirecting the treatment can improve outcomes for women who have STEMI. We need more representation of women in trials regarding cardiovascular disease to identify possible associations that might have an impact in mortality.

## Conflicts of interest

None.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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