[b]Facultad de Ciencias Biosanitarias, Universidad Francisco de Vitoria, Madrid, Spain
[c]Servicio de Cardiología, Hospital Universitario de la Princesa, Madrid, Spain
[d]Servicio de Oftalmología, Hospital Universitario de Torrejón, Torrejón de Ardoz, Madrid, Spain
[e]Servicio de Cardiología, Hospital General Universitario Gregorio Marañón, Madrid, Spain
[f]Facultad de Ciencias Biomédicas y de la Salud, Universidad Europea, Madrid, Spain
[g]Facultad de Medicina, Universidad Complutense, Madrid, Spain

* Corresponding author:
E-mail address: j.ruizgarcia@hotmail.com (J. Ruiz-García).

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Iron Deficiency in Patients With Acute Coronary Syndrome: Prevalence and Predisposing Factors

Déficit de hierro en pacientes con síndrome coronario agudo: prevalencia y factores predisponentes

To the Editor,

Iron deficiency (ID), with or without anemia, is a prevalent comorbidity in patients with chronic heart failure that confers a worse outcome.[1,2] There are no data on the prevalence of ID development or its associated factors in acute coronary syndrome (ACS).

Here, we present a descriptive analysis of patients admitted to our center for ACS. This analysis forms part of a prospective registry of patients with ACS that will be used, once patient inclusion and follow-up have been completed, to analyze the prognostic implication of this comorbidity in this clinical setting. The following patients were excluded: those who refused to provide informed consent, those referred to another center during admission, those who died in the first 5 days after the ACS, and those who had major bleeding or received treatment with blood derivatives or iron. Inflammatory parameters (ultrasensitive C-reactive protein and interleukin-6 [IL 6]) and iron metabolism data were determined at 5 and 30 days. In line with the international consensus, ID was defined as ferritin < 100 ng/mL or as ferritin < 800 ng/mL if transferrin saturation was $< 20\%$. After patient inclusion, data were collected on demographic and clinical variables potentially involved in ID development.

A total of 139 patients (age, 67 ± 14 years; 32% women) were included between November 2012 and June 2014. Of these, 85 (61%) had ID and 39 (28%) had anemia. These rates decreased to 54% and 23% among the 119 patients whose analytical determinations were performed at 30 days. Patients with ID had higher blood glucose, lower hemoglobin (Hb), and higher C-reactive protein and IL-6 concentrations ($P \leq .01$) (Table). No differences were found in the proportion of ACS with ST elevation, distribution of coronary lesions, and treatment received during hospitalization.

Multivariable logistic regression analysis showed that IL-6 ($P = .011$), Hb on admission ($P = .001$), and pretreatment with aspirin ($P = .021$) were independent predictors of ID.

Table
Clinical and Treatment Characteristics of Patients With Acute Coronary Syndrome With and Without Iron Deficiency

	Without ID (n = 54)	With ID (n = 85)	*P*
Men	42 (78)	53 (62)	.06
Age, y	64 ± 13	70 ± 14	.02
Cardiovascular risk factors			
Diabetes mellitus	9 (17)	29 (34)	.03
Hypertension	28 (52)	67 (79)	.01
Dyslipidemia	28 (52)	45 (57)	.60
Smoking	23 (42)	18 (21)	<.01
Medical history			
Previous coronary heart disease	10 (19)	23 (27)	.17
Previous heart failure	1 (2)	3 (4)	.23
COPD	5 (9)	14 (17)	.31
Anemia	2 (4)	12 (14)	.04
Renal failure	5 (9)	14 (17)	.31
Chronic treatment			
Aspirin	7 (13)	31 (37)	<.01
Other antiplatelet agents	3 (6)	4 (5)	.56
Anticoagulants	5 (9)	6 (7)	.44
Beta-blockers	8 (15)	20 (24)	.28
ACEIs	13 (24)	30 (35)	.11

Table *(Continued)*
Clinical and Treatment Characteristics of Patients With Acute Coronary Syndrome With and Without Iron Deficiency

	Without ID (n = 54)	With ID (n = 85)	*P*
Statins	20 (37)	34 (40)	.43
Type of ACS			
STEACS	32 (59)	46 (54)	.34
Clinical parameters			
Heart rate, bpm	74 ± 16	75 ± 19	.73
SBP at admission, mmHg	137 ± 27	138 ± 31	.17
Blood glucose at admission, mg/dL	135 ± 50	164 ± 66	< .01
Hb at admission, g/dL	14.5 ± 1.4	13.6 ± 1.6	< .01
Cr at admission, mg/dL	0.88 ± 0.27	0.88 ± 0.32	.78
Maximum usTnT, ng/L	934 [210-2961]	1287 [261-4932]	.32
LVEF, %	55 ± 9	54 ± 11	.66
Killip II-IV	5 (9)	13 (15)	.31
Procedures performed			
Laboratory tests during admission	6.6 ± 1.5	6.7 ± 1.9	.66
Coronary angiography	50 (93)	72 (85)	.19
Angioplasty	41 (76)	59 (71)	.44
Coronary heart disease			
Left main coronary artery involvement	4 (7)	5 (6)	.69
Three-vessel involvement	6 (11)	14 (16)	.22
Treatment received during admission			
Aspirin	54 (100)	83 (98)	.52
Clopidogrel	37 (70)	54 (79)	.31
Other antiplatelet agents	41 (76)	52 (61)	.15
Low-molecular-weight heparin	43 (80)	64 (75)	.35
Acenocoumarol	3 (5)	7 (8)	.41
Beta-blockers	49 (91)	82 (97)	.15
ACEI	47 (87)	66 (77)	.12
Statins	54 (100)	85 (100)	
Inflammatory state on the 5th day			
usCRP, mg/dL	0.9 [0.4-2]	1.4 [0.5-4.9]	.014
IL-6, pg/mL	6.3 [3.9-10.4]	10.4 [5.8-17.4]	< .001

ACS, acute coronary syndrome; ACEIs, angiotensin-converting enzyme inhibitors; COPD, chronic obstructive pulmonary disease; Cr, creatinine; Hb, hemoglobin; ID, iron deficiency; IL-6, interleukin 6; LVEF, left ventricular ejection fraction; renal failure, glomerular filtration < 60 mL/min/1.73 m^2; SBP, systolic blood pressure; STEACS, ST elevation acute coronary syndrome; usCRP, ultrasensitive C-reactive protein; usTnT, ultrasensitive troponin T.
The data are expressed as n (%), mean ± standard deviation, or median [interquartile range].

The present study showed a high ID prevalence in ACS (61%). This high prevalence also persisted in more than half of the patients 30 days after the coronary event. Both findings are novel and only comparable in the context of ischemic heart disease with the series of Jankowska et al,[3] which reported the presence of ID in 48% of patients with stable coronary artery disease undergoing cardiac surgery. The association between ID and ACS could have unknown prognostic implications in quality of life and long-term functional capacity.

The small sample size and short follow-up do not permit clarification of the prognostic impact of ID on ACS, limiting the clinical implications of our findings until the conclusion of patient inclusion and follow-up. Neither is analysis possible of the pathophysiological mechanisms causing ID in the setting of ACS. However, the independent association between ID and chronic aspirin therapy, low Hb values, and a heightened inflammatory state (high levels of IL-6 and C-reactive protein) is alarming.

More specifically, the relationship between ID and inflammatory status has been seen in patients with advanced chronic heart failure.[4] In contrast, a previous study by our group found that patients with a more heightened inflammatory status admitted for ACS had a higher probability of anemia development during hospitalization.[5] Our data are in accordance with those of Huang et al,[6] who showed a significant association between low serum iron and high IL-6 concentrations in patients with ST elevation ACS. As is well known, inflammation plays a role in atherosclerotic plaque formation, and inflammatory status is more pronounced at the time of plaque rupture. It seems plausible, although still speculative, that coronary heart disease (and, more specifically, its decompensation) and ID would show common etiopathogenic mechanisms related to this inflammatory status, beyond a possible etiopathogenic association per se between ID and ACS.

The most likely cause of the association between ID and chronic aspirin therapy is undetected chronic gastrointestinal bleeding. However, it is unclear whether the possible development of ID indicates a need to modify the antiplatelet strategy in these patients.

In conclusion, ID is a prevalent and persistent condition in ACS associated with chronic antiplatelet therapy, anemia, and a heightened inflammatory status, with unknown prognostic implications.

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CONFLICTS OF INTEREST

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Oona Meroño,[a,*] Mercé Cladellas,[b] Núria Ribas-Barquet,[c] Lluís Recasens,[c] Víctor Bazán,[c] and Josep Comín-Colet[b]

[a]*Departamento de Cardiología, Grupo de Investigación Biomédica en Enfermedades del Corazón, IMIM (Instituto de Investigación del Hospital del Mar), Doctorate, Universidad Autónoma de Barcelona, Hospital del Mar, Barcelona, Spain*
[b]*Departamento de Cardiología, Grupo de Investigación Biomédica en Enfermedades del Corazón, IMIM (Instituto de investigación del Hospital del Mar), Hospital del Mar, Barcelona, Spain*
[c]*Departamento de Cardiología, Hospital del Mar, Barcelona, Spain*

[*] Corresponding author:
E-mail address: 98605@parcdesalutmar.cat (O. Meroño).

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Circulatory Support With Extracorporeal Membrane Oxygenation System as a Bridge to Heart Transplantation in Complex Postinfarction Ventricular Septal Rupture

Asistencia circulatoria con oxigenador extracorpóreo de membrana como puente a trasplante cardiaco en rotura septal ventricular compleja

To the Editor,

The optimal timing for surgery to treat mechanical complications of acute myocardial infarction is still under debate.[1]

Postinfarction ventricular septal defect (VSD) is an infrequent complication associated with high mortality. The actual incidence of this condition ranges from 0.17% to 0.31%, with a mortality of 94% with medical treatment and 42.5% with surgery.[1] The variables associated with greater mortality are age, need for early surgery, size > 12 mm, and posterior site.[2]

Recently, the potential use of circulatory support systems as a bridge to definitive correction of postinfarction VSD or even as a bridge to heart transplantation has been reported.[3]

This article presents the first reported experience in Spain of extracorporeal membrane oxygenation (ECMO) as a bridge to heart transplantation in a patient with 2 mechanical complications of myocardial infarction: a large posterior VSD and left ventricular pseudoaneurysm.

The patient was a 62-year-old man with hypertension and type 2 diabetes mellitus. He presented with a 14-hour history of oppressive chest pain.

The electrocardiogram showed Q waves with 2-mm ST elevation in the lower leads and 1.5-mm ST depression in the lateral leads. Blood pressure was 110/50 mmHg and he had sinus tachycardia at 120 bpm. On physical examination, a pansystolic III/VI murmur was noted at the left sternal border.

Emergent coronary angiography was performed using the right radial artery approach. This showed involvement of the right coronary system with complete occlusion of the mid segment of the right coronary artery (Figure 1A). Left ventriculography showed an undilated left ventricle (LV), with inferior akinesia and a posterior spherical cavity filled with contrast in the same phase as the LV, and subsequent passage of contrast to the right ventricle (Figure 1B and video in the supplementary material). An intra-aortic balloon pump was implanted. Echocardiography revealed an undilated LV with a large VSD (Figure 2A) at the level of the posterior and basal segments of the septum, with left-right flow and diameters of 30 x 23 mm. The ventricular wall also showed severe thinning in these segments consistent with pseudoaneurysm. Neither pericardial effusion nor valve disease was observed, and right ventricular function was preserved.

Given the large extent and the posterior site of the VSD, the lesion was considered surgically irreparable. It was therefore decided to implant an ECMO device as circulatory support using the left femoral artery approach. The patient was placed on a waiting list for heart transplantation with top priority (Figure 2B). On the third day, successful heart transplantation was performed without any complications. The patient's postoperative recovery was free of complications and he was discharged after 15 days.

Study of the explanted heart confirmed the diagnoses; a large VSD was observed in the basal and posterior part of the septum and, related to this, a posterior pseudoaneurysm within the visceral pericardium (Figure 2B).

This article presents the first reported experience in Spain of ECMO device implantation as a bridge to heart transplantation in an unusual case with 2 mechanical complications of myocardial infarction considered surgically irreparable. ECMO is used increasingly frequently in situations of refractory cardiogenic shock[4] and as circulatory support for high-risk coronary intervention.[5] Recently, the feasibility of implanting such devices in the catheterization laboratory has been reported.[6]

We believe that the use of this type of peripheral circulatory support in complex mechanical complications of myocardial infarction such as large VSD in our present patient is preferable to longer-term ventricular assist devices, as the procedure is less