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Original article

In-hospital Acquired Anemia in Acute Coronary Syndrome. Predictors, In-hospital Prognosis and One-year Mortality

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ABSTRACT

Introduction and objectives: Anemia at hospital admission predicts a poor outcome in patients presenting with acute coronary syndrome. It remains unclear whether in-hospital hemoglobin levels decrease (nosocomial anemia) not related to bleeding also implies a poor prognosis. We aimed to identify predictors of nosocomial anemia and its prognostic significance.

Methods: We prospectively included 221 acute coronary syndrome patients admitted in our institution during the years 2009-2010, with normal hemoglobin levels at admission. Nosocomial anemia was defined as a decrease in hemoglobin levels to <13g/dL in men and <12g/dL in women in the absence of apparent bleeding. Clinical variables and hematological inflammatory parameters were assessed in order to identify predictors for the development of nosocomial anemia. We compared the clinical outcome after a 1-year follow-up period of patients without anemia as opposed to those who developed nosocomial anemia.

Results: Nosocomial anemia was registered in 25% of study patients. A >3.1 mg/dL value of C-reactive protein was highly predictive of developing nosocomial anemia (odds ratio=5.9; 95% confidence interval, 2.6-13.4; *P*<.001). The incidence of mortality and cardio-vascular morbidity was higher in the patients who developed nosocomial anemia (34.5% vs 9%; *P*<.001). Nosocomial anemia was a strong predictor of cardio-vascular morbidity and mortality in the long-term follow-up (hazard ratio=2.47; 95% confidence interval, 1.23-4.96; *P*=.01).

Conclusions: Nosocomial anemia predicts a poorer outcome in patients with acute coronary syndrome. Increased C-reactive protein levels, indicating inflammatory state, are predictive of developing in-hospital anemia unrelated to apparent bleeding.

Anemia adquirida en el síndrome coronario agudo. Predictores, pronóstico intrahospitalario y mortalidad a un año

Palabras clave:
Anemia adquirida intrahospitalaria
Anemia nosocomial
Síndrome coronario agudo
Pronóstico
Estado inflamatorio

RESUMEN

Introducción y objetivos: La anemia al ingreso por un síndrome coronario agudo es un factor de mal pronóstico. Sin embargo, hay poca información sobre la anemia que se adquiere durante el ingreso por un síndrome coronario. Nuestro objetivo es determinar posibles predictores de anemia nosocomial y evaluar su influencia pronóstica en el síndrome coronario agudo.

Métodos: Se incluyó prospectivamente a 221 pacientes que ingresaron en nuestro centro por un síndrome coronario (2009-2010) con valores de hemoglobina normales. Se definió anemia nosocomial sin sangrado evidente como reducción de hemoglobina a valores < 13 g/dl en varones y < 12 g/dl en mujeres. Se analizó el pronóstico a 1 año de seguimiento comparando a los pacientes con anemia nosocomial con los que se mantuvieron sin anemia. Se excluyó del análisis a los pacientes con complicaciones hemorrágicas.

Resultados: Se observó anemia nosocomial en el 25% de los pacientes. El análisis multivariable reveló una asociación entre proteína C reactiva > 3,1 mg/dl y aparición de anemia nosocomial (*odds ratio* = 5,9; intervalo de confianza del 95%, 2,6-13,4; p < 0,001). Al año de seguimiento, el 34,5% de los pacientes con anemia nosocomial habían sufrido complicaciones cardiovasculares y/o muerte, frente al 9% de los que se mantuvieron sin anemia (p < 0,001). La anemia nosocomial resulta ser un predictor potente de mortalidad total y de complicaciones cardiovasculares (*hazard ratio* = 2,47; intervalo de confianza del 95%, 1,23-4,96; p = 0,01).

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Conclusiones: La anemia nosocomial sin sangrado evidente es un predictor de morbimortalidad a largo plazo. Un estado inflamatorio más marcado, indicado por la proteína C reactiva > 3,1 mg/dl, puede predecir la aparición de anemia durante la hospitalización.

Abreviaturas

ACS: acute coronary syndrome
CRP: C-reactive protein
Hb: hemoglobin

INTRODUCTION

Anemia at hospital admission in patients presenting with acute coronary syndrome (ACS) varies between 15% and 43% according to some series[1–3] and leads to increased in-hospital and long-term morbidity and mortality.[3–6] There is little information on in-hospital anemia among patients with ACS. Salisbury et al.[7] suggest that up to 57.5% of patients admitted with normal hemoglobin (Hb) values acquire anemia during hospital admission. Patients with so-called "nosocomial anemia" also have higher morbidity and mortality during 1-year follow-up than those who maintain normal Hb values,[8] although bleeding complications may influence the prognosis of these patients. Bleeding in patients with ACS is not negligible and is partly due to antiplatelet and anticoagulant therapy and invasive procedures. However, the causes of nosocomial anemia in patients without apparent bleeding during hospital stay are poorly understood and, according to some series, up to 86.5% of patients with acquired anemia do not have documented bleeding.[8] Only a small number of authors have suggested repeated blood samples as a possible cause.[9,10] On the other hand, an inflammatory state in ACS has been described,[11–13] although no information is available on the influence of inflammation on the development of anemia in patients with ACS.

The aims of our study were to analyze the possible causes of nosocomial anemia in the absence of apparent bleeding, identify clinical and hematologic predictors, and assess their influence on the prognosis of patients with ACS.

METHODS

During 2009-2010, 302 patients with ACS (with or without ST-segment elevation) were consecutively admitted to our hospital's coronary care unit. Patients with anemia at admission were excluded from the analysis (n=70) as well as patients with bleeding complications during the hospital stay (n=11). Bleeding was defined as all intracranial or clinically evident bleeding that was the cause of death or hypotension or that required intravenous treatment, surgical intervention, or red blood cell transfusion.[14,15] Finally, the study group consisted of 221 patients with ACS with normal Hb values at admission and no apparent bleeding during hospitalization.

We prospectively collected clinical and epidemiological variables such as age, sex, cardiovascular risk factors, and other comorbidities. Complete blood count and biochemical analysis were performed at the time of arrival at the emergency department, serial analyses of markers of myocardial necrosis were performed at 6 h and 12 h, and a complete blood count at 8 am after admission. The amount extracted and time of extraction of further blood samples was left to the discretion of the attending physician. We recorded the number of tests performed, the Hb values at admission and during hospitalization, the number of white blood cells (WBC) at admission and the maximum peak observed. We measured ultrasensitive C-reactive protein (CRP) values during the first 24 h of admission, with a median time from hospital arrival of 16.7 h [interquartile range, 10.2-20.2 h]. The treatments administered and procedures performed were also recorded. The patients were classified into 2 groups: group 1 consisted of those with nosocomial anemia and group 2 included those who maintained normal Hb values during their entire hospital stay. We compared prognosis between the 2 groups during 1-year follow-up. Finally, we performed a subanalysis to assess the possible prognostic impact of a decrease in Hb>2/dL during admission, comparing the course of patients who had decreases>2/dL to those who did not.[16] A single observer conducted follow-up by a review of medical records and telephone follow-up.

Definitions

The Hb value at admission was defined as the first Hb value obtained and anemia at admission was defined as a baseline Hb value <13/dL in men and <12/dL in women. Nosocomial anemia without apparent bleeding was defined as a decrease during hospitalization of Hb values to <13/dL in men and <12/dL in women after they had been admitted with normal Hb values and with no evidence of any type of bleeding or bleeding complication. CRP values were used to analyze the association between anemia and inflammation, as this is the prototypical acute phase reactant that reflects systemic inflammation and has been widely validated as a marker of cardiovascular risk; these values begin to increase 8 h after the onset of symptoms of infarction.[17,18] Patients with CRP>3.1mg/dL (75th percentile of our series) were considered to have more pronounced inflammation.[19–22] The definition of heart failure was based on clinical or radiological evidence of pulmonary venous congestion according to the Killip classification.[23] Kidney failure was defined as serum creatinine>1.5/dL.[24] The GRACE score was used to stratify the risk of ACS.[25,26] Left ventricular systolic function was estimated by echocardiography or ventriculography. Nonfatal cardiovascular complications during follow-up were grouped in a composite endpoint consisting of the onset of a new ACS, stroke, or admission for heart failure. Cardiovascular mortality was defined as mortality due to ACS, heart failure, ventricular arrhythmia, or stroke.

Statistical Analysis

Continuous variables were expressed as mean (standard deviation) or as median [interquartile range] if they did not follow the normal distribution. Discrete variables were expressed as the absolute number and percentage. Clinical differences were analyzed using the *t*-test for independent data and percentages were analyzed using the chi-square test and Fisher's exact test when appropriate.

Logistic regression analysis was performed to determine the potential association of the variables with the occurrence of nosocomial anemia.[27] The results are expressed as odds ratio (OR) with a 95% confidence interval (95%CI). We performed a receiver-operating characteristic (ROC) curve analysis to verify that the prediction model was optimal. Kaplan-Meier curves were constructed to compare inter-group patient survival to the composite endpoint of cardiovascular complications and mortality using the log rank test. Multivariate analysis was performed using Cox regression (saturated model) to establish which were the best determinants of survival. Covariates that reached marginal statistical significance ($P<.10$) were introduced in the bivariate analysis. Subsequently, the variables were included one by one if their exclusion did not significantly alter the likelihood ratio model. If their exclusion changed more than 15% of the variable under study, this was considered a confounding effect and the variable was kept in the model. The results are expressed as hazard ratio (HR) with 95%CI. The variables age, heart rate, baseline systolic blood pressure, baseline blood glucose, baseline Hb value, ejection fraction, peak WBCs count, and number of hospital days were included as continuous variables in the multivariate analyses. Maximum Killip class (taking Killip III-IV as a potential predictor), GRACE score (taking indicator 1 as moderate risk and indicator 2 as high risk), diabetes, nosocomial anemia and CRP>3.1/dL were included as discrete variables.

A *P*-value of <.05 was used as a cutoff for statistical significance; all analyzes were performed using the SPSS software package version 18.

RESULTS

Of the study patients admitted for ACS with normal Hb values, 25% (group 1, 55 patients) had anemia with no evidence of bleeding during hospitalization. Table 1 shows the demographic characteristics, comorbidities and admission data of the 2 groups.

Patients who had nosocomial anemia were older (67.6 vs 60.3: $P<.001$) and had more chronic kidney failure (7.2% vs 1.2%; $P=.04$). They also had lower systolic blood pressure values at admission (136 vs 147; $P=.04$) and more elevated markers of myocardial necrosis (troponin T, 4.3 μg/L vs 2.4μg/L; $P=.002$). In group 1, the percentage of patients with infarctions in Killip III-IV was higher (21.8% vs 3.6%; $P<.001$) and their stay in the coronary care unit was longer (3.2 vs 2.1; $P=.02$). Coronary angiography was performed in 80.9% of patients with ST-segment elevation ACS and in 82.5% of patients with non-ST-segment elevation ACS. There were no significant inter-group differences in the number of coronary arteries affected. Angioplasty was performed in 71% of patients with ST-segment elevation ACS and 50% of patients with non-ST-segment elevation ACS. There were no significant inter-group differences in the medical treatment administered or the number of patients in whom the central or arterial access routes, balloon counterpulsation, or mechanical ventilation were used. Table 2 shows the treatments administered, techniques employed, and hospital outcome. There were no significant differences in the number of days of hospitalization (7.8 days in group 1 and 7.2 days in group 2; $P=.3$).

Table 3 shows the changes in Hb values. The baseline mean Hb value was 15.0/dL and 13.6/dL for men and women, respectively. The baseline mean Hb value in group 1 was 14.0/dL vs 14.9/dL in group 2 ($P<.001$). The mean decrease in Hb value during hospitalization in group 1 was 2.5/dL (18%) vs 0.9/dL (6%) in group 2 ($P<.001$). Only 5 patients (9.1%) with nosocomial anemia had a minimum Hb value<10/dL. There were no differences between groups in the number of blood tests performed.

Table 1
Baseline Characteristics and Admission Data

	Group 1[a] (n=55)	Group 2[b] (n=166)	*P*
Men	37 (67.3)	129 (77.7)	.150
Age, years	67.6±13	60.3±13	<.001
Risk factors			
Diabetes	16 (29.1)	30 (18.1)	.080
Hypertension	35 (63.6)	94 (56.6)	.520
Dyslipidemia	34 (61.8)	87 (52.4)	.350
Smoking	24 (43.6)	81 (48.8)	.850
Comorbidities			
COPD	8 (14.5)	17 (10.2)	.150
Vasculopathy	2 (3.6)	14 (8.4)	.370
Stroke	2 (3.6)	4 (2.4)	.640
CKD	4 (7.2)	2 (1.2)	.040
Admission data			
Baseline HR, bpm	84±22	78±20	.050
Baseline SBP, mmHg	136±33	147±31	.040
Baseline glucose, mg/dL	154±80	133±56	.030
Cr at admission, mg/dL	1.2±1.1	1.0±0.9	.250
CRP, mg/dL	5.7±0.8	2.4±0.2	<.001
Average maximum white blood cells, cells/μL	12 828	11 420	<.010
Type of ACS			.230
ST-segment elevation	27 (49.1)	68 (40.9)	
Non-ST-segment elevation	28 (50.9)	98 (59.1)	
EF, %	45±12	55±12	<.001
GRACE score			<.001
Low risk	7 (12.7)	52 (31.3)	
Moderate risk	10 (18.2)	58 (35.0)	
High risk	38 (69.1)	56 (33.7)	

ACS, acute coronary syndrome; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CRP, C-reactive protein; EF, ejection fraction; HR, heart rate; SPB, systolic blood pressure.
[a] Patients with in-hospital anemia without apparent bleeding.
[b] Patients without in-hospital anemia.

Table 2
Procedures, Medical Treatment and In-hospital Course

	Group 1[a] (n=55)	Group 2[b] (n=166)	*P*
Procedures			
Coronary angiography	45 (81.8)	134 (80.7)	.800
Angioplasty	31 (56.4)	99 (59.6)	.800
Treatments			
Acid acetilsalicilic	53 (96.4)	160 (96.4)	.400
Clopidogrel	53 (96.4)	166 (100)	1
Heparin	54 (98.1)	165 (99.4)	.200
Glycoprotein-IIb/IIIa inhibitors	9 (16.3)	37 (22.3)	.600
Beta blockers	46 (83.6)	144 (86.7)	.800
ACEI	42 (76.4)	121 (72.9)	.900
Statins	54 (98.1)	164 (98.7)	1
Fibrinolytics	3 (5.5)	11 (6.6)	1
In-hospital course			
Killip class III-IV	12 (21.8)	6 (3.6)	<.001
Hospital mortality	1 (1.8)	3 (1.8)	.600

ACEI, angiotensin-converting enzyme inhibitors.
Data are expressed as no. (%).
[a] Patients with in-hospital anemia without apparent bleeding.
[b] Patients without in-hospital anemia.

Table 3
Changes in Hemoglobin Values and Number of Extractions

	Group 1[a] (n=55)	Group 2[b] (n=166)	*P*
Changes in hemoglobin values			
Baseline hemoglobin, g/dL	14±1.3	14.9±1.3	<.001
Men	14.5±1.2	15.1±1.2	
Women	13±0.9	13.9±0.9	
Minimum hemoglobin, g/dL	11.5±1.0	13.9±1.1	<.001
Men	11.8±1.0	14.2±1.0	
Women	10.9±0.8	14.1±1.0	
Decrease in hemoglobin, %	18	6	
Number of extractions	6.7±2.4	6.2±1.7	.300
≤5%	41.8	39.8	
6-7%	36.4	33.1	
>7%	21.8	27.1	

Unless otherwise indicated, data are expressed as mean±standard deviation.
[a] Patients with in-hospital anemia without apparent bleeding.
[b] Patients without in-hospital anemia.

Table 4
Multivariate Logistic Regression Analysis. Independent Association of C-Reactive Protein With Anemia. First Model

	OR (95%CI)	*P*
CRP>3.1/dL	4.59 (1.89-11.16)	.001
Baseline hemoglobin	0.62 (0.44-0.87)	.006
Moderate-risk GRACE score	0.65 (0.19-2.31)	.510
High-risk GRACE score	2.64 (0.77-9.00)	.121
Women	0.98 (0.39-2.45)	.957
Age	1.00 (0.97-1.04)	.848

95%CI, 95% confidence interval; CRP, C-reactive protein; OR, odds ratio.

The univariate analysis showed that 36.4% of patients in group 1 had CRP values>3.1/dL, whereas only 10.2% of patients in group 2 had similar CRP values. The multivariate analysis (Table 4) demonstrated an association between CRP>3.1/dL and the development of in-hospital anemia (OR=5.9; 95%CI, 2.59-13.41; *P*<.001). The other predictor of onset of anemia was the Hb value at admission, although this association was weaker (OR=0.58; 95%CI, 0.43-0.77; *P*<.001) than the association with CRP values. No significant associations were observed regarding the other variables studied. The area under the ROC curve was 0.85 (95%CI, 0.79-0.92) for the model developed, with acceptable calibration (Hosmer-Lemeshow test, *P*=.343).

Table 5
Events During Follow-up

	Group 1[a] (n=55)	Group 2[b] (n=166)
Cardiovascular events	19	12
ACS		
Fatal	6	4
Nonfatal	5	0
Admission for HF		
Fatal	0	0
Nonfatal	7	5
Stroke		
Fatal	0	1
Nonfatal	1	2
VF (mortal)	1	0

ACS, acute coronary syndrome; HF, heart failure; VF, ventricular fibrillation.
[a] Patients with in-hospital anemia without apparent bleeding.
[b] Patients without in-hospital anemia.

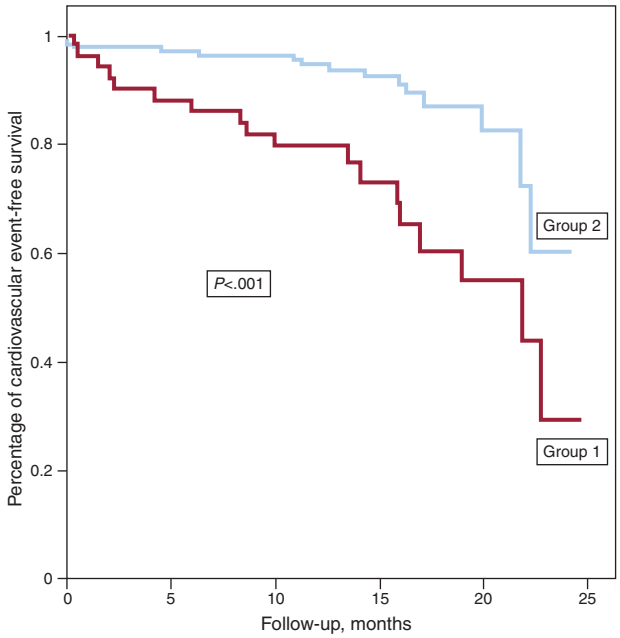

Figure. Survival curve for the combined endpoint of total mortality and cardiovascular complications.

The median follow-up of patients was 13.6 months [10.2 to 17.4 months]. In total, 5.8% of patients were lost to follow-up. Table 5 shows complications during follow-up. There were 12 (21.8%) patients with cardiovascular complications in group 1 and 10 (6.0%) patients in group 2 (*P*=.003). Regarding cardiovascular mortality, there were 7 (12.7%) deaths in group 1 and 10 (3%) deaths in group 2 (*P*=.01). Figure shows the survival curves for the composite endpoint. The multivariate analysis (Table 6) demonstrated that nosocomial anemia was associated with the composite endpoint (HR=2.47; 95%CI, 1.23-4.96; *P*=.01). The other variable associated with poor prognosis was age (HR=1.07; 95%CI, 1.03-1.11; *P*<.001).

Assessment of an Absolute Decrease>2/dL in Hemoglobin Values

To assess the potential prognostic effect of a decrease in Hb values>2/dL during admission, independently of whether this

Table 6
Cox Multivariate Regression Analysis. Adjusted Effect of Anemia on the Composite Endpoint. First Model

	HR (95%CI)	*P*
Nosocomial anemia	2.39 (1.11-5.19)	.027
Moderate-risk GRACE score	0.89 (0.16-4.95)	.892
High-risk GRACE score	1.59 (0.30-8.41)	.583
Age	1.06 (1.02-1.10)	.007
Baseline glucose level	1.00 (0.99-1.00)	.456
Women	0.79 (0.37-1.71)	.554

95%CI, 95% confidence interval; HR, hazard ratio.

Table 7
Data of Patients With and Without Decreased Hemoglobin Values>2/dL

	Decrease >2/dL (n=48)	Decrease ≤2/dL (n=173)	*P*
Men	37 (77.1)	129 (74.6)	.850
Age, years	63.9±14	61.7±13	.340
Admission data			
Baseline HR, bpm	85±23	77±19	.030
CRP >3.1/dL	14 (29.8)	23 (15.5)	.040
CRP, mg/dL	3.9±0.8	1.5±0.2	<.001
Average maximum white blood cells, cells/μL	13 690	10 866	<.001
Hb at admission, mg/dL)	14.6±1.2	15.1±1.5	.010
Minimum Hb, mg/dL	12±1.5	13.7±1.3	<.001
Troponin T, μg/L	4.6±0.7	2.3±0.3	<.001
EF, %	47±12	54±12	<.010
GRACE score			.020
Low risk	14 (29.2)	45 (26)	
Moderate risk	7 (14.6)	61 (35.3)	
High risk	27 (56.2)	67 (38.7)	
Type of ACS			.020
ST-segment elevation	28 (58.3)	67 (38.7)	
Non-ST-segment elevation	20 (41.7)	106 (61.3)	
Killip class III-IV	9 (19.1)	9 (5.6)	.010

ACS, acute coronary syndrome; CRP, C-reactive protein; EF, ejection fraction; Hb, hemoglobin; HR, heart rate.
Data are expressed as no. (%) or mean±standard deviation.

led to nosocomial anemia or not, we performed a bivariate analysis comparing the data of patients with decreases in Hb>2/dL to those of patients who did experience this decrease. Table 7 shows the variables in which differences were found between groups. In the multivariate analysis of survival, a decrease in Hb values>2/dL was not associated with an increased risk of events.

DISCUSSION

Our study shows that nosocomial anemia in patients with ACS without apparent bleeding is a frequent complication (25%) and a predictor of mortality and cardiovascular complications during the first year of follow-up. In our series, patients in group 1 had slightly lower baseline Hb values than those in group 2, although in both groups these values were >14/dL. In patients with nosocomial anemia, the decrease in Hb values was three times greater than that of patients who did not have anemia. Although the degree of documented anemia was slight, we found that acquired anemia has prognostic significance since the average minimum Hb value detected in the group with nosocomial anemia was 11.5/dL and only 9.1% of the patients in this group had Hb values<10 g/dL. This variation in Hb values during hospitalization is consistent with the values reported in other studies.[7,28]

Regarding the additional multivariate analysis conducted to analyze the relative decrease in Hb values in relation to prognosis, we found that decreases in Hb values>2/dL during admission did not lead to a higher rate of cardiovascular complications or cardiovascular mortality during follow-up. We therefore propose an Hb value<13/dL in men and <12/dL in women as an appropriate cutoff value to predict a worse prognosis in these patients.

There are several mechanisms by which anemia occurs in patients hospitalized for ACS. By excluding patients who presented anemia at admission, we eliminated the causes of chronic anemia (chronic kidney failure, gastrointestinal bleeding, autoimmune disease, hematopoietic stem cell deficiency, etc.), and in this way the patients who developed anemia during hospital stay were selected. The most obvious cause of nosocomial anemia is bleeding complications, which have been suggested as independent factors of poor prognosis in patients with ACS.[29,30] In our series, we excluded patients with hemorrhagic complications in order to analyze the causes and consequences of nosocomial anemia of unknown origin (in our sample, 90.2% of patients with acquired anemia). Repeat blood samples have been suggested as a possible cause of nosocomial anemia without apparent bleeding during hospitalization.[9,10,31] In our series, no differences were found in the number of blood samples extracted between the 2 groups, thus eliminating this as a possible cause of nosocomial anemia.

By analyzing different variables as predictors of nosocomial anemia in patients without apparent bleeding, we found that the patients with anemia had higher CRP values at admission. This suggests an association between elevated CRP values and the development of in-hospital anemia, given the higher probability of anemia in patients with CRP values>3.1/dL than in those with lower CRP values. A more pronounced inflammatory state could explain the occurrence of nosocomial anemia, since in some patients with ACS there would be an increase in circulating cytokines that would suppress erythropoiesis, thereby blocking iron stores and inhibiting intestinal absorption.[32] One hypothesis is that in some patients, and due to specific individual characteristics, a myocardial lesion might trigger a greater inflammatory cascade leading not only to adverse cardiac and hemodynamic outcomes, but also to poor absorption and use of nutrients. This would initiate the suppression of erythropoiesis and lead to anemia a few days after myocardial damage had occurred. This hypothesis of a more pronounced inflammatory state would be supported by the fact that in the anemic patients infarctions were more extensive (greater troponin T values), with a greater percentage of heart failure and lower ejection fraction values (Table 1). The presence of an inflammatory state, its effect on iron metabolism and its role in iron deficiency (absolute or functional) in the prognosis of patients with heart failure have recently been studied.[33–36] We have found no reports on this topic in patients with ACS. Therefore, further studies are needed on the type of iron metabolism impairment during the acute phase of ACS and its prognostic impact. Similarly, a second phase should assess the possible treatment options for nosocomial anemia in the absence of bleeding, for example, the effect of iron supplementation, whose benefit has been demonstrated in patients with heart failure.[37]

In our study, the baseline Hb value was associated with the occurrence of nosocomial anemia, although this association was weaker than that between CRP values and nosocomial anemia. Most of the literature reviewed on this topic suggests that patients without anemia at admission but with baseline Hb values in the lower percentiles are the patients most likely to acquire anemia. It follows that minor variations in Hb values would lead to these patients being classified within the nosocomial anemia group. Other possible causes of anemia, such as sex or age, showed no significant association in our study.

As in the SIESTA study,[38,39] we found that the CRP value was not an independent marker of morbidity and mortality. In our series, an elevated CRP value was shown to be a powerful predictor of nosocomial anemia without apparent bleeding.

In view of our results, and taking into account that low levels of anemia may be overlooked in clinical practice despite having great

prognostic relevance, changes in Hb values should be monitored. To this end, it may be advisable to implement clinical protocols in which the number of blood samples and their time of extraction are recorded. These protocols should include the CRP values as an indicator of the degree of inflammation. In patients with elevated CRP values, monitoring Hb values would have even greater importance. Other studies would also be needed to determine the most appropriate treatment of nosocomial anemia.

Limitations

In this study, we conducted a combined analysis of patients with ACS with and without ST-segment elevation, diseases that are not treated and managed in exactly the same way. However, no significant differences were found in the distribution of the type of ACS between the 2 groups or in prognosis during follow-up according to whether or not the patients had ST elevation. Given that the patients with anemia at admission were not analyzed to exclude causes of chronic anemia, some cases of subacute anemia may have been excluded, but our specific interest was to determine the causes of nosocomial anemia. By excluding patients with bleeding complications, we could not analyze the prognostic impact of these complications nor that of blood transfusions, although many studies have shown that in anemic patients they lead to an even worse prognosis.[29,30] Unfortunately, we could not obtain information on the exact volume of blood extracted per sample, and thus we cannot ensure that the amount of blood extracted was exactly the same in both groups. Despite this, we consider that the number of tests conducted is a good approach, albeit indirect, to estimate the amount of blood extracted. Other factors that could result in the onset of anemia, such as hydration status or the number of venous access routes and their location, were not recorded in our study.

CONCLUSIONS

This study demonstrates that nosocomial anemia without apparent bleeding in patients with ACS is a frequent complication (25%) and a predictor of mortality and cardiovascular complications during the first year of follow-up. Our results show that this phenomenon is associated with a marked inflammatory state, indicated by CRP values>3.1/dL, which are predictive of the development of in-hospital anemia. In our study, nosocomial anemia was not associated with an excess of blood samples extracted during admission.

CONFLICTS OF INTEREST

None declared.

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