Prevalence and prognostic significance of anemia in patients presenting for ST-elevation myocardial infarction in a Tunisian center

Walid Jomaa a,⇑, Imen Ben Ali a, Sonia Hamdi a, Mohamed A. Azaiez a, Aymen El Hraïech a, Khaldoun Ben Hamda a, Faouzi Maatouk a

a Cardiology B Department, Fattouma Bourguiba University Hospital and University of Monastir, Monastir
a Tunisia

Background: Anemia on admission is a powerful predictor of major cardiovascular events in patients presenting for acute coronary syndromes. We sought to determine the prevalence and prognostic impact of anemia in patients presenting for ST-elevation myocardial infarction (STEMI).

Methods: We analyzed data from a Tunisian retrospective single center STEMI registry. Patients were enrolled between January 1998 and October 2014. Anemic and nonanemic patients were compared for clinical and prognostic features and according to four prespecified hemoglobin level subgroups. In patients with severe anemia, factors associated with in-hospital death were studied.

Results: A total of 1498 patients were enrolled. Mean age was 60.47 ± 12.7 years and prevalence of anemia was 36.6%. Anemic patients were more likely to be elderly, hypertensive, and diabetic in comparison to nonanemic patients. In-hospital mortality was significantly higher in anemic patients (14.9% vs. 5%, \( p < 0.001 \)). Lower hemoglobin levels were significantly associated with a higher prevalence of heart failure on admission, cardiogenic shock, and in-hospital mortality (\( p < 0.001 \) for all). In univariate analysis, factors associated with in-hospital death in patients with severe anemia were hypertension (\( p = 0.044 \)), heart failure on admission (\( p < 0.001 \)), renal failure on admission (\( p < 0.001 \)), and primary percutaneous coronary intervention (pPCI) use (\( p = 0.016 \)). The absence of pPCI use was independently associated with in-hospital death in multivariate analysis (odds ratio = 2.22, 95% confidence interval: 1.07–4.76, \( p = 0.033 \)).

Conclusion: According to this study, anemic patients presenting for STEMI have a higher in-hospital mortality rate. The absence of pPCI use was independently associated with in-hospital death.

© 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Keywords: Anemia, Mortality, Primary percutaneous coronary intervention, ST-elevation myocardial infarction

Disclosure: Authors have nothing to disclose with regard to commercial support.

Received 10 May 2016; revised 30 September 2016; accepted 9 October 2016.
Available online 20 October 2016

⇑ Corresponding author at: Cardiology B Department, Fattouma Bourguiba University Hospital, Avenue 1er juin, 5000 Monastir, Tunisia.
E-mail address: jomaa_w@hotmail.fr (W. Jomaa).
1. Introduction

Anemia at presentation and during hospital stay is reported to be highly predictive of poor in-hospital and long-term outcomes in patients presenting with acute coronary syndromes (ACS) [1–4]. In several reports, baseline hemoglobin level was proven to be correlated to the incidence of in-hospital complications in patients treated for ST-elevation myocardial infarction (STEMI) [5–7]. Furthermore, blood transfusion is a frequently utilized therapeutic in this setting and was nevertheless proven to be another predictor of adverse events in patients hospitalized for ACS [8,9].

Aside from hemoglobinopathies in the younger demographic, iron-deficiency accounts for the majority of anemia cases in the adult population in the Middle East and North Africa [10–12]. In addition, it is also known that the epidemiology of STEMI with regards to patients risk profile and management strategies implemented are quite different in these parts of the world when compared to those in Western countries. In many of these countries, indeed, the implementation of primary percutaneous coronary intervention (pPCI) for the management of STEMI is still not the default strategy and an evaluation of the impact of anemia at presentation on outcomes, especially in relation to the management strategies adopted, is warranted. No data from the North African countries are available.

In this study, we sought to investigate the prevalence and the prognostic significance of anemia on admission in patients presenting with STEMI in a Tunisian tertiary care center, particularly in relation to therapeutic strategies utilized in this context.

2. Materials and methods

2.1. Population and study design

The present study was led on data from the STEMI registry of Cardiology B Department, Fattouma Bourguiba University Hospital (Monastir, Tunisia). The registry enrolls in a yearly fashion all patients aged ≥18 years presenting to our center for STEMI, regardless of the management strategy adopted. The study performed is a retrospective observational study on all consecutive patients admitted to our department between January 1998 and October 2014. Patients are referred to our department from the emergency ward or the local Emergent Medical Aid system. The diagnosis of STEMI was established in the presence of a significant ST-segment elevation (1 mm in frontal leads and 2 mm in precordial leads) in two adjacent leads, or a presumably new left bundle branch block concomitantly to a persistent (>20 minutes) chest discomfort. In our practice, the decision to perform pPCI, thrombolysis, or not to opt for a reperfusion therapy is undertaken as in accordance as possible with the European Society guidelines [13], while taking into account the ischemic-hemorrhagic balance for each reperfusion modality, implementation delays, and the patient clinical background. Reasons for managing patients conservatively (i.e., without reperfusion) were diverse (late presentation, advanced age, etc.). All patients received intravenously 100 UI/kg of weight unfractionated heparin upon diagnosis, 250 mg aspirin and a 300-mg or 600-mg loading dose of clopidogrel according to the reperfusion strategy chosen (thrombolysis or pPCI).

Clinical history and cardiovascular risk factors were collected upon presentation and at 24 hours. Initial physical examination was reported. Blood samples were retrieved upon admission for blood cell count and other standard analyses. Anemia was defined according to the World Health Organization criteria (hemoglobin <13 g/dL in men and <12 g/dL in women) [14]. Severe anemia was defined by a hemoglobin rate <11 g/dL. Anemic and nonanemic patients were first compared regarding clinical characteristics, management, and in-hospital complications and mortality; the study population was then split into four prespecified subgroups according to baseline hemoglobin levels (≥16 g/dL, 13.5–15.9 g/dL, 11–13.4 g/dL, and <11 g/dL) to better analyze trends in clinical and prognostic features according to the hemoglobin subgroup. Heart failure (HF) on admission was...
defined by a Killip II or Killip III class. Killip IV class was referred to as cardiogenic shock. Renal failure on admission was defined as a creatinine clearance <45 mL/min using the Modification of Diet in Renal Disease formula in patients not previously known to suffer from chronic kidney disease (CKD); in patients known to have CKD, renal failure on admission was defined as an increase of ≥30% of baseline serum creatinine rate. Bleeding complications were defined as any overt or nonovert bleeding with a drop of ≥2 g/dL in hemoglobin or needing blood transfusion. In patients with severe anemia, relevant factors associated with in-hospital death were studied in univariate then in multivariate analysis.

2.2. Statistical analysis
Continuous variables were presented as means ± standard deviation. Categorical variables are presented as absolute values and percentages. When appropriate, the chi-square test was applied to compare proportions between anemic and nonanemic patients and between the four prespecified hemoglobin subgroups. It was also applied to determine factors associated with in-hospital death in univariate analysis. Mean values of continuous variables were compared between anemic and nonanemic patients using the Student t test. In the four subgroup analysis, the difference between means was evaluated using the one way analysis of variance test. Multivariate analysis on variables significantly associated with in-hospital death in univariate analysis was performed using binary logistic regression. Results are expressed as odds ratios (OR) with accompanying 95% confidence interval (95% CI). A p value <0.05 was considered significant. Statistical analyses were performed using SPSS (SPSS Inc, Chicago, IL, USA) version 17 for Windows.

3. Results
The overall study population included 1498 patients. Five hundred and forty-four (36.3%) patients were anemic. Prevalence of anemia was comparable between women and men (38.4% vs. 35.7%, p = 0.36) and significantly higher in elderly compared to younger patients (52.1% vs. 34.8%, p < 0.001). Compared to nonanemic patients, anemic patients were more likely to have a history of arterial hypertension (p < 0.001) and diabetes mellitus (p = 0.007) (Table 1). Conversely, they

### Table 1. Clinical characteristics and in-hospital course in anemic patients versus nonanemic patients presenting for ST-elevation myocardial infarction (STEMI).

|                          | Population (n = 1498) | Nonanemic (n = 954) | Anemic (n = 544) | p       |
|--------------------------|-----------------------|---------------------|------------------|---------|
| Age (y)                  | 60.47 ± 12.7          | 58 ± 12.5           | 64.71 ± 11.83    | <0.001  |
| Age > 75 y               | 211 (15%)             | 101 (11.5%)         | 110 (21%)        | <0.001  |
| Female gender            | 333 (22.2%)           | 205 (21.5%)         | 128 (23.5%)      | 0.361   |
| Hypertension             | 451 (30.1%)           | 245 (25.7%)         | 206 (37.9%)      | <0.001  |
| Diabetes mellitus        | 534 (35.6%)           | 316 (33.1%)         | 218 (40.1%)      | 0.007   |
| Current smoker           | 1000 (66.8%)          | 678 (71.1%)         | 322 (59.2%)      | <0.001  |
| Dyslipidemia             | 177 (12.1%)           | 115 (12.2%)         | 62 (11.9%)       | 0.869   |
| Obesity                  | 190 (12.7%)           | 132 (13.9%)         | 58 (10.7%)       | 0.071   |
| History of HF            | 34 (2.3%)             | 18 (1.9%)           | 16 (2.9%)        | 0.188   |
| History of PCI           | 122 (8.1%)            | 87 (9.1%)           | 35 (6.4%)        | 0.068   |
| History of CABC          | 6 (0.4%)              | 5 (0.5%)            | 1 (0.2%)         | 0.316   |
| HF on admission          | 331 (22.1%)           | 195 (20.4%)         | 136 (25%)        | 0.041   |
| Cardiogenic shock on admission | 35 (2.3%) | 13 (1.4%)         | 22 (4%)          | 0.001   |
| Renal failure on admission | 116 (8.3%)      | 40 (4.6%)           | 76 (14.5%)       | <0.001  |
| Anterior infarction      | 696 (46.5%)           | 454 (47.6%)         | 242 (44.5%)      | 0.247   |
| Primary PCI              | 424 (28.3%)           | 280 (29.4%)         | 144 (26.5%)      | 0.234   |
| Symptoms to primary PCI delay (h) | 4.88 ± 4.23 | 4.6 ± 3.85         | 5.39 ± 4.81      | 0.071   |
| Thrombolysis             | 510 (34%)             | 348 (36.5%)         | 162 (29.8%)      | 0.009   |
| Symptoms to thrombolysis delay (h) | 3.79 ± 4.23 | 3.44 ± 3.35         | 4.5 ± 5.11       | 0.004   |
| No reperfusion therapy   | 564 (37.6%)           | 326 (34.1%)         | 238 (43.7%)      | 0.001   |
| New onset atrial fibrillation | 100 (6.7%)       | 60 (6.3%)           | 40 (7.4%)        | 0.428   |
| Inotropic agents use     | 216 (14.4%)           | 113 (11.8%)         | 103 (18.9%)      | <0.001  |
| Bleeding complication    | 41 (2.8%)             | 24 (2.5%)           | 17 (3.2%)        | 0.473   |
| CUC length of stay (d)   | 4.74 ± 3.55           | 4.7 ± 3.1           | 4.79 ± 4.22      | 0.667   |
| In-hospital mortality    | 129 (8.6%)            | 48 (5%)             | 81 (14.9%)       | <0.001  |

CABG = coronary artery bypass grafting; CCU = coronary care unit; HF = heart failure; PCI = percutaneous coronary intervention.
were less likely to be current smokers ($p < 0.001$). Regarding clinical presentation, anemic patients were more likely to experience HF ($p = 0.041$), renal failure ($p < 0.001$), and cardiogenic shock ($p = 0.001$) on admission. No statistical difference could be reported regarding pPCI use as the reperfusion option for STEMI between anemic and nonanemic patients. By contrast, recourse to thrombolysis was significantly lower in the anemic group (29.8% vs. 36.5%, $p = 0.009$). Likewise, mean delay between symptoms onset and thrombolysis was significantly longer. Recourse to inotropic agents was more frequent in anemic patients, whereas no difference in the occurrence of bleeding complications was noticed between the two groups. Anemia was associated with a significantly higher in-hospital mortality rate (14.9% vs. 5% in nonanemic patients, $p < 0.001$).

Investigating population clinical characteristics and outcomes according to baseline hemoglobin levels (Table 2) revealed a gradual increase in mean age with lower hemoglobin levels. Prevalence of elderly, female gender, hypertension, and diabetes was significantly higher in the lower hemoglobin subgroups. A progressive increase in the occurrence of HF and cardiogenic shock upon presentation was noted in lower hemoglobin subgroups and so was the recourse to inotropic agents use. No significant ascending or descending trend for bleeding complications occurrence or in the mean coronary care unit length of stay could be seen across the hemoglobin level spectrum. In-hospital mortality was by far the highest (22.1%) in the severe anemia subgroup (hemoglobin $<11$ g/dL) compared to 6.4% (in the hemoglobin $\geq 16$ g/dL subgroup), 3.5% (in the hemoglobin

| Table 2. Clinical presentation and in-hospital course in patients presenting for ST-elevation myocardial infarction (STEMI) according to four hemoglobin level subgroups. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Age (y)                         | Group 1 Hb $\geq 16$ g/dL (n = 110) | Group 2 Hb 13.5–15.9 g/dL (n = 600) | Group 3 Hb 11–13.4 g/dL (n = 539) | Group 4 Hb < 11 g/dL (n = 249) |
| Age > 75                        | 55.35 ± 11.05   | 56.88 ± 12.48   | 62.77 ± 12.15   | 66.52 ± 11.67   |
| Female gender                   | 5 (4.5%)        | 55 (9.2%)       | 90 (16.7%)      | 65 (26.1%)      |
| Hypertension                    | 94 (15.7%)      | 135 (25%)       | 102 (41%)       | 93 (37.3%)      |
| Diabetes mellitus               | 19 (17.3%)      | 139 (23.2%)     | 201 (37.3%)     | 112 (45%)       |
| Tobacco smoking                 | 27 (14.8%)      | 331 (61.4%)     | 114 (45.8%)     | $<0.001$       |
| HF on-admission                 | 101 (91.8%)     | 454 (75.7%)     | 311 (64.1%)     | $<0.001$       |
| Cardiogenic shock               | 2 (1.8%)        | 11 (2%)         | 15 (6%)         | $<0.001$       |
| Renal failure on admission      | 3 (2.7%)        | 40 (7.4%)       | 50 (20%)        | $<0.001$       |
| Primary PCI                     | 31 (28.2%)      | 154 (28.6%)     | 60 (24.1%)      | 0.41           |
| Symptoms to primary PCI delay   | 5.38 ± 6.09     | 4.53 ± 3.75     | 4.75 ± 4.11     | 5.97 ± 4.63     |
| Thrombolysis                    | 49 (44.5%)      | 189 (35.1%)     | 62 (24.9%)      | 0.002          |
| Symptoms to thrombolysis delay  | 3.7 ± 3.94      | 4.08 ± 4.76     | 4.98 ± 6.21     | 0.009          |
| No reperfusion therapy          | 30 (27.3%)      | 196 (36.3%)     | 127 (51%)       | 0.001          |
| Bleeding complication           | 4 (3.7%)        | 12 (2%)         | 10 (4.1%)       | 0.357          |
| Inotropic agents use            | 16 (14.5%)      | 74 (13.7%)      | 67 (26.9%)      | $<0.001$       |
| CCU Length of stay              | 4.91 ± 2.76     | 4.72 ± 3.4      | 4.98 ± 5.11     | 0.626          |
| In-hospital mortality           | 7 (6.4%)        | 46 (8.5%)       | 55 (22.1%)      | $<0.001$       |

CCU = coronary care unit; Hb = hemoglobin; PCI = percutaneous coronary intervention.

Table 3. Relevant factors associated with in-hospital death in patients with severe anemia presenting for ST-elevation myocardial infarction (STEMI) in univariate analysis.

| Factor                          | Surviving | Dead | $p$   |
|---------------------------------|-----------|------|-------|
| Female gender                   | 69 (35.6%)| 24 (43.6%)| 0.275 |
| Age < 75 y                      | 49 (25.3%)| 16 (29.1%)| 0.568 |
| Hypertension                    | 73 (37.6%)| 29 (52.7%)| 0.044 |
| Diabetes mellitus               | 85 (42.8%)| 29 (52.7%)| 0.191 |
| HF on admission                 | 47 (24.2%)| 29 (52.7%)| $<0.001$ |
| Renal failure on admission      | 27 (14.8%)| 23 (41.8%)| $<0.001$ |
| Primary PCI                     | 40 (20.6%)| 20 (36.4%)| 0.016 |
| New onset atrial fibrillation   | 15 (7.7%) | 10 (18.2%)| 0.023 |

HF = heart failure; PCI = percutaneous coronary intervention.
1.07–4.76, death in multivariate analysis (OR = 2.22, 95% CI: 1.73–6.74, death were HF on admission (OR = 3.42, 95% CI: 1.73–6.74, <0.001). Multivariate analysis performed on this model showed that factors independently associated with in-hospital mortality were studied (Table 3). In univariate analysis, factors significantly associated with in-hospital mortality in patients with severe anemia were hypertension (p = 0.044), HF on admission (p < 0.001), renal failure on admission (p < 0.001), new onset atrial fibrillation (p = 0.023), and pPCI as a reperfusion strategy (p = 0.016). Multivariate analysis performed on this model showed that factors independently associated with in-hospital death were HF on admission (OR = 3.42, 95% CI: 1.73–6.74, p < 0.001), and renal failure on admission (OR = 3.82, 95% CI: 1.83–7.96, p < 0.001). The absence of pPCI use as the reperfusion option was independently associated with in-hospital death in multivariate analysis (OR = 2.22, 95% CI: 1.07–4.76, p = 0.033) (Table 4).

### 4. Discussion

This is an original study performed in a North African country that clearly highlights the prognostic impact of baseline anemia in patients presenting for ACS and in particular acute STEMI. Furthermore, the study emphasizes the heavy prognostic impact of clinical presentation in severely anemic patients and the beneficial effect of pPCI in these critically ill patients.

In the present study, prevalence of anemia in patients presenting for STEMI was 36.3%. This rate is considerably higher than those reported in western series. Al Falluji et al. [1] reported a prevalence of 10.2% in a large American database from New Jersey and Tsujita et al. [4] found similar rates in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial [4]. In the Middle Eastern Gulf RACE II registry [15], this prevalence rose to 28% in patients presenting for ACS but remained lower than that reported in our study.

The impact that anemia has on in-hospital course in patients presenting for STEMI has been confirmed in several studies and irrespectively of the antithrombotic regimens and reperfusion modalities used [4,16,17]. Results from the present study regarding the harmful effect of anemia in these patients are in accordance with those reported elsewhere. Such an effect could be due to anemia itself, but also to other comorbid conditions classically associated with it that could aggravate the former effect or be a confounding factor such as renal failure. Likewise, the prognostic significance of low baseline hemoglobin levels was consistent in a variety of demographic groups and clinical settings. Kitai et al. [18] demonstrated an impact of low hemoglobin levels on mortality in patients undergoing pPCI that was maintained even for those with mild anemia. In the same study, a concomitant CKD was associated with significantly higher incidence of major cardiovascular events. In our study, the relationship between baseline hemoglobin level and the occurrence of HF or cardiogenic shock upon presentation was obvious. Recourse to inotropic agents had also the same trend. In the Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan (OPTIMAAL), anemia was associated with HF on presentation and there was a clear trend to higher Killip classes in STEMI with lower hemoglobin levels [19]. In a study carried out in 2310 patients presenting for ACS in the United Kingdom, Archbold et al. [6] identified anemia as a powerful determinant of clinically diagnosed left ventricular dysfunction occurrence with the highest rates in STEMI and for the lowest hemoglobin categories. In another report, on top of being predictive of overall mortality, anemia was also predictive of mortality from noncardiac causes in young patients [20].

In-hospital mortality rate was significantly higher in anemic patients in comparison to nonanemic ones and was particularly high in patients with severe anemia (22.1%). This fact could be demonstrated in several reports, but in our study, the in-hospital mortality rate in anemic patients is generally higher. In our context, these patients have a higher prevalence of traditional

Table 4. Factors independently associated with in-hospital death in patients with severe anemia presenting for ST-elevation myocardial infarction (STEMI) in multivariate analysis.

| Variable                      | Odds ratio | 95% CI      | p     |
|-------------------------------|------------|-------------|-------|
| Hypertension                  | 1.66       | 0.83–3.29   | 0.148 |
| Diabetes mellitus             | 1.3        | 0.64–2.60   | 0.458 |
| HF on admission               | 3.42       | 1.73–6.74   | <0.001|
| Renal failure on admission    | 3.82       | 1.83–7.96   | <0.001|
| Primary PCI                   | 0.45       | 0.21–0.93   | 0.033 |
| New onset atrial fibrillation | 0.44       | 0.16–1.2    | 0.112 |

CI = confidence interval; HF = heart failure; PCI = percutaneous coronary intervention.
cardiovascular risk factors and other comorbidities when compared to Western populations, which could partly explain such a disparity in outcomes.

There are several pathophysiological explanations to the worse clinical outcome and mortality in patients suffering from coronary artery disease and anemia. In anemic patients, there is a significant reduction of oxygen supply to the myocardium in addition to the impaired coronary blood flow. Other mechanisms include tachycardia and decrease in blood viscosity [21]. Eventually, recourse to blood transfusion in anemic patients with or without hemorrhagic complications was proven to be a powerful predictor of worse outcome in the whole ACS spectrum [9].

In our current practice, reperfusion strategies (i.e., thrombolysis and pPCI) were not equally utilized according to hemoglobin subgroups. While there was a significant trend to less thrombolysis use in patients with lower baseline hemoglobin levels, pPCI was equally used in the different subgroups. This propensity to a less recurrent recourse to reperfusion therapies in anemic patients was frequently reported in the literature [22,23]. Operators often prefer not to opt for an invasive procedure or hemorrhage-inducing pharmacological therapeutic in patients at risk of bleeding. In our study, in patients with severe anemia, the use of pPCI as the reperfusion option was associated with a worse in-hospital outcome in univariate analysis. In our context, the decision to perform (or not) a pPCI is left to the discretion of the operator, and in all likelihood this led to a subpopulation with a critical clinical presentation and outcome. Nonetheless and interestingly, this observation was reversed when pPCI was included in a multivariate model where its effect on in-hospital mortality was adjusted to main variables associated with the latter outcome. This is a highly informative result given that it emphasizes the beneficial effect of pPCI in STEMI even for patients suffering from severe anemia for whom such a procedure could be considered hazardous at a first glance.

4.1. Study limitations

Although very informative about our current practice, the present study was performed on data that were collected retrospectively in a periodical manner and the results have to be interpreted very cautiously. No randomization was carried out and compared subgroups cannot perfectly match regarding all variables linked with risk profile and prognosis. Results certainly cannot be extrapolated to the whole Tunisian population given that the study was performed on a near exclusively urban population. Another study limitation is the absence of relation between the hemoglobin levels and the occurrence of hemorrhagic events during hospital stay. Indeed, prevalence of bleeding complications was low and statistical significance precisely in this topic could probably be reached in a larger study population.

5. Conclusion

The present study issued from a single center registry confirms the high prevalence of anemia in patients presenting for STEMI in the Tunisian context. In these patients, low baseline hemoglobin levels were significantly associated with worse in-hospital outcomes. In patients with severe anemia, initial clinical presentation was very impactful on in-hospital outcomes and the absence of pPCI use as a reperfusion therapy was independently associated with in-hospital death.

References

[1] Al Falluji N, Lawrence-Nelson J, Kostis JB, Lacy CR, Ranjan R, Wilson AC. Myocardial infarction data acquisition system (MIDAS #8) study group. Effect of anemia on 1-year mortality in patients with acute myocardial infarction. Am Heart J 2002;144:636–41.
[2] Sabatine MS, Morrow DA, Giugliano RP, Burton PB, Murphy SA, McCabe CH, et al.. Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. Circulation 2005;111:2042–9.
[3] Shu DH, Ransoms TP, O’Connell CM, Cox JL, Kaiser SM, Gee SA, et al.. Anemia is an independent risk for mortality after acute myocardial infarction in patients with and without diabetes. Cardiovasc Diabetol 2006;5:8.
[4] Tsujita K, Nikolsky E, Lansky AJ, Dangas G, Fahy M, Brodie BR, et al.. Impact of anemia on clinical outcomes of patients with ST-segment elevation myocardial infarction in relation to gender and adjunctive antithrombotic therapy (from the HORIZONS-AMI trial). Am J Cardiol 2010;105:1385–94.
[5] Lipsic E, van der Horst IC, Voors AA, van der Meer P, Nijsten MW, van Gilst WH, et al.. Hemoglobin levels and 30-day mortality in patients after myocardial infarction. Int J Cardiol 2005;100:289–92.
[6] Archbold RA, Balami D, Al-Hajiri A, Suliman A, Liew R, Cooper J, et al.. Hemoglobin concentration is an independent determinant of heart failure in acute coronary syndromes: cohort analysis of 2310 patients. Am Heart J 2006;152:1091–5.
[7] Aronson D, Suleiman M, Agmon Y, Suleiman A, Blich M, Kapeliovich M, et al.. Changes in haemoglobin levels during hospital course and long-term outcome after acute myocardial infarction. Eur Heart J 2007;28:1289–96.
[8] Rao SV, Jollis JG, Harrington RA, Granger CB, Newby LK, Armstrong PW, et al.. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA 2004;292:1555–62.
[9] Chatterjee S, Wetterslev J, Sharma A, Lichstein E, Mukherjee D. Association of blood transfusion with increased mortality in myocardial infarction: a meta-analysis and diversity-adjusted study sequential analysis. JAMA Int Med 2013;173:132–9.
[10] Al Zenki S, Alomirah H, Al Hooti S, Al Hamad N, Jackson RT, Rao A, et al.. Prevalence and determinants of anemia and iron deficiency in Kuwait. Int J Environ Res Publ Health 2015;12:9036–45.

[11] Khosrof-Ben Jaâfar S, Gharbi N, El Fazaâ S, Beji C, Farhat A, Cherif S, et al.. Iron deficiency anemia and proteino-energetic status in woman from 15 to 49 years old in Tunisia. Tunis Med 2004;82:263–70 [in French].

[12] Chebbi W, Arfa S, Zantour B, Sfar MH. Iron deficiency anemia in people aged 65 years and older: a cohort study of 102 patients. Rev Med Brux 2014;35:405–10 [in French].

[13] Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), European Association for Percutaneous Cardiovascular Interventions (EAPCI), Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al.. Guidelines on myocardial revascularization. Eur Heart J 2010;31:2501–55.

[14] World Health Organization. Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. Geneva, Switzerland: World Health Organization; 2001. Available at: <http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en/index.html> (accessed 20.01.2016).

[15] Sulaiman K, Prashanth P, Al-Zakwani I, Al-Mahmeed W, Al-Motarreb A, Al Suwaidi J, et al.. Impact of anemia on in-hospital, one-month and one-year mortality in patients with acute coronary syndrome from the Middle East. Clin Med Res 2012;10:65–71.

[16] Nikolsky E, Aymong ED, Halkin A, Grines CL, Cox DA, García E, et al.. Impact of anemia in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: analysis from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial. J Am Coll Cardiol 2004;44:547–53.

[17] Rousseau M, Yan RT, Tan M, Lefkowitz CJ, Casanova A, Fitchett D, et al.. Integrilin and enoxaparin randomized assessment of acute coronary syndrome treatment (INTERACT) trial investigators. Relation between hemoglobin level and recurrent myocardial ischemia in acute coronary syndromes detected by continuous electrocardiographic monitoring. Am J Cardiol 2010;106:1417–22.

[18] Kitai Y, Ozasa N, Morimoto T, Bao B, Furukawa Y, Nakagawa Y, et al.. CREDO-Kyoto registry investigators. Prognostic implications of anemia with or without chronic kidney disease in patients undergoing elective percutaneous coronary intervention. Int J Cardiol 2013;168:5221–8.

[19] Anker SD, Voors A, Onkonk D, Clark AL, James MK, von Haehling S, et al.. Prevalence, incidence, and prognostic value of anaemia in patients after an acute myocardial infarction: data from the OPTIMAAL trial. Eur Heart J 2009;30:1331–9.

[20] Ariza-Solé A, Formiga F, Salazar-Mendiguchía J, Garay A, Lorente V, Sánchez-Salado JC, et al.. Impact of anaemia on mortality and its causes in elderly patients with acute coronary syndromes. Heart Lung Circ 2015;24:557–65.

[21] Bassand JP. Impact of anaemia, bleeding, and transfusions in acute coronary syndromes: a shift in the paradigm. Eur Heart J 2007;28:1273–4.

[22] Valeur N, Nielsen OW, McMurray JJ, Torp-Pedersen C, Kober L, et al.. Anaemia is an independent predictor of mortality in patients with left ventricular systolic dysfunction following acute myocardial infarction. Eur J Heart Fail 2006;8:577–84.

[23] Meneveau N, Schiele F, Seronde MF, Descotes-Genon V, Oettinger J, Chopard R, et al.. Anemia for risk assessment of patients with acute coronary syndromes. Am J Cardiol 2009;103:442–7.