#### ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

# Impact of anaemia on long-term outcomes in patients treated with first- and second-generation drug-eluting stents; Katowice-Zabrze Registry

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#### Abstract

**Background:** Coexisting anaemia is associated with an increased risk of major adverse cardiac and cerebrovascular events (MACCE) and bleeding complications after percutaneous coronary intervention (PCI), especially in patients with acute coronary syndrome.

**Aim:** To assess the impact of anaemia in patients with coronary artery disease (CAD) treated with first- and second-generation drug-eluting stents (DES) on one-year MACCE.

Methods and results: The registry included 1916 consecutive patients (UA: n = 1502, 78.3%; NSTEMI: n = 283, 14.7%; STEMI/LBBB: n = 131, 6.8%) treated either with first- (34%) or second-generation (66%) DES. The study population was divided into two groups: patients presenting with anaemia 217 (11%) and without anaemia 1699 (89%) prior to PCI. Anaemia was defined according to World Heart Organisation (haemoglobin [Hb] level < 13 g/dL for men and < 12 g/dL for women). Patients with anaemia were older (69, IQR: 61-75 vs. 62, IQR: 56-70, p < 0.001), had higher prevalence of co-morbidities: diabetes (44.7% vs. 36.4%, p = 0.020), chronic kidney disease (31.3% vs. 19.4%; p < 0.001), peripheral artery disease (10.1% vs. 5.4%, p = 0.005), and lower left ventricular ejection fraction values (50, IQR: 40-57% vs. 55, IQR: 45-60%; p < 0.001). No difference between gender in frequency of anaemia was found. Patients with anaemia more often had prior myocardial infarction (MI) (57.6% vs. 46.4%; p = 0.002) and coronary artery bypass grafting (31.3% vs. 19.4%; p < 0.001) in comparison to patients without anaemia. They also more often had multivessel disease in angiography (36.4% vs. 26.1%; p = 0.001) and more complexity CAD as measured by SYNTAX score (21, IQR: 12-27 points vs. 14, IQR: 8-22 points; p = 0.001). In-hospital risk of acute heart failure (2.7% vs. 0.7%; p = 0.006) and bleeding requiring transfusion (3.2% vs. 0.5%; p < 0.001) was significantly higher in patients with anaemia. One-year follow-up showed that there was higher rate of death in patients with anaemia. However, there were no differences in MI, stroke, target vessel revascularisation (TVR) and MACCE in comparison to patients with normal Hb. There were no differences according to type of DES (first vs. second generation) in the population of patients with anaemia.

**Conclusions:** In patients with anaemia there is a significantly higher risk of death in 12-month follow-up, but anaemia has no impact on the incidence of MI, repeat revascularisation, stroke and MACCE. There is no advantage of II-DES over I-DES generation in terms of MACCE and TVR in patients with anaemia.

Key words: percutaneous coronary intervention, drug eluting stents, anaemia

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#### **INTRODUCTION**

Coronary artery disease (CAD) continues to be the most common cause of death in middle-aged and elderly individuals in developed countries. In addition to the well-known risk factors such as age, male-gender, smoking, dyslipidaemia, and impaired glucose tolerance, haematological disorders seem also to play an important role in the progression of CAD. Anaemia is the one of the most common haematological abnormalities observed in patients with CAD, occurring in 15-19% of patients with acute coronary syndromes (ACS) [1, 2] and in 24.6% of patients undergoing primary percutaneous coronary intervention (PCI) [3]. The combination of CAD and anaemia leads to increased mortality and higher incidence of major adverse cardiac and cerebrovascular events (MACCE) in patients referred for revascularisation [4-6]. Furthermore, in those patients, drug-eluting stent (DES) implantation and one type of corrective therapy for CAD appears to increase the risk of bleeding due to prolonged dose of double antiplatelet therapy (DAPT). However, the registry of Shishehbor et al. [7] demonstrated that, regardless of the haemoglobin (Hb) level, DES implantation reduced MACE and mortality in patients with mild-to-moderate anaemia, as compared to bare-metal stent implantation. Stent technology has also progressed from first-generation DES (I-DES) to second-generation DES (II-DES). Since both generational DES types are in use, this can influence the outcomes observed from this therapy. Currently, there is limited data that assess the impact of DES types (I-DES vs. II-DES) on PCI outcomes in patients with anaemia. Moreover, those patients are often excluded from randomised clinical studies. According to the PRODIGY study, the use of II-DES was associated with a lower risk of cumulative MACCE as compared to I-DES [8] in the general population. The goal of this study was to assess the impact of anaemia on clinical outcomes in the population of patients treated with PCI with DES, and to observe in patients with anaemia any differences in outcomes, between patients with II-DES implantation compared with patients who received I-DES implantation.

## METHODS Study population

The all-comer, independent Katowice-Zabrze retrospective registry provided data on 1916 consecutive patients treated with either first- (paclitaxel, sirolimus eluting; 34%) or second-generation (everolimus, zotarolimus, biolimus A9, 66%) DES. The enrolment was conducted in two cardiac centres, 3<sup>rd</sup> Department of Cardiology, Katowice-Ochojec, and the 2<sup>nd</sup> Department of Cardiology, Zabrze Silesian Medical University of Katowice, Poland from January 2009 to December 2010. Baseline characteristics, cardiac history, risk factors, medications, and angiographic and procedural data were also obtained and recorded. Anaemia was diagnosed based on the level of Hb on admission to the hospital. Primary

efficacy end-point was MACCE defined as death, stroke, or target vessel revascularisation (TVR) were recorded in all patients at one-year follow-up. Angiographic data were collected on all patients undergoing PCI and recorded in the Cardiovascular Information Registry. SYNTAX score was calculated for all patients without prior coronary artery bypass grafting (CABG). Data regarding long-term outcomes (mortality and MACCE) were extracted from the main database of the National Health Fund.

#### Statistical analysis

Statistical analysis was performed using MedCalc software (v.12 Belgium). Quantitative variables are presented as mean  $\pm$  standard deviation and median with interquartile range (IQR; Q1–Q3). Qualitative data is expressed as crude values and/or percentages. Between-group differences were assessed using Mann-Whitney U test for quantitative variables and  $\chi^2$  test for qualitative variables. Data distribution was verified with Smirnow-Kolmogorov test. Kaplan-Meier curves were used to present the unadjusted time-to-event data for investigated end-points. Additionally, multivariable modelling was performed using Cox proportional hazards method to assess the adjusted association between all end-points and DES type. All tests were two-tailed. P < 0.05 was considered significant.

### RESULTS Demographics

During 24 months 1916 patients were admitted with final diagnosis as follows: unstable angina (UA) 1502 (78%), non-ST-segment elevation myocardial infarction (NSTEMI) 238 (15%), and ST-segment elevation myocardial infarction (STEMI)/left bundle branch block [LBBB]) 131 (7%). Patients were treated either with first- (paclitaxel, sirolimus) or second-generation (everolimus, zotarolimus, biolimus A9) DES (I-DES = 645; II-DES = 1271). There were 680 (35.5%)females and 1236 (64.5%) males. Anaemia, as defined by the World Health Organisation was Hb level < 13 g/dL for men and < 12 g/dL for women [9], was present in 217 (11%) patients (137 [65%] men and 80 [37%] women; p = 0.708). According to the mean corpuscular volume (MCV), the most common type of anaemia was normocytic (MCV from 80 fL to 100 fL) 53%, macrocytic (MCV > 100 fL) 35%, and the least common type was microcytic (MCV < 80 fL) 11%. In the total population of ACS patients, the median Hb level was 14 (IQR: 13–16 g/dL), and respective values for STEMI/LBBB, NSTEMI, and UA were 14.7, IQR: 13.4-16.6; 14.2, IQR: 13.0-16.2; 14.1, IQR: 13.3–16.1 g/dL, respectively.

#### Comorbidities and chronic medications

Patients with anaemia were older (69, IQR: 61-75 vs. 62, IQR: 56-70 years; p < 0.001), had higher prevalence of co-morbidities: diabetes (44.7% vs. 36.4%, p = 0.020), chronic

obstructive pulmonary disease (COPD) (10.1% vs. 5.5%; p = 0.009), peripheral artery disease (PAD) (10.1% vs. 5.4%; p = 0.005), higher creatinine level (p < 0.001), and had higher Global Registry of Acute Coronary Events (GRACE) risk scores over 140 points (72.7% vs. 53.1%; p = 0.010). They also more often had prior myocardial infarction (MI) (57.6% vs. 46.4%; p = 0.002) and CABG (31.3% vs. 19.4%; p < 0.001) in comparison to patients without anaemia. Clinical presentation was different across the spectrum of patients. Patients with anaemia were admitted more often with higher heart rate (75, IQR: 65-80 vs. 70, IQR: 60-78 bpm; p = 0.010), andno difference was observed in the systolic blood pressure at admission (130, IQR: 120-145 vs. 130, IQR: 120-150 mm Hg; p = 0.301) than in patients with normal Hb levels. Patients with anaemia and ACS were admitted more often with higher Killip class, as shown in Table 1. According to the medical treatments, they more often received oral anticoagulation (8.3% vs. 4.4%; p = 0.013). There was no difference in peri- and post-procedural medical treatment in both groups.

#### Left ventricular function

Left ventricular ejection fraction (LVEF) values were available in 98.7% of all study patients. In the general population LVEF was normal in 70% of patients, moderately reduced (31–50%) in 24%, and severely ( $\leq$  30%) reduced in 6% of patients. Patients with anaemia had lower LVEF values compared to patients with normal Hb levels (p < 0.001) (Table 1).

#### Interventional treatment and reperfusion strategy

Subsequent analyses revealed that the populations of patients with and without anaemia differ in the complexity of coronary atherosclerotic lesions. Patients with anaemia more often had multi-vessel disease in angiography (36.4% vs 26.1%, p = 0.001) and more complexity CAD as measured by SYN-TAX score (21, IQR: 12–27 vs. 14, IQR: 8–22, p = 0.001). They had more complex lesions (B/C) and less frequent simple type A. In angiography patients with anaemia also had more significant stenosis of left main (22.1% vs. 11.6%; p < 0.001), left circumflex (65.9% vs. 53.4%; p < 0.001), right coronary artery (61.8% vs. 34.4%; p = 0.020), and arterial by-pass graft (9.2% vs. 4.5%; p < 0.002). First- and second-generation DES were implanted with similar frequency in patients with and without anaemia (Table 2).

#### In-hospital outcomes

There was a significantly higher rate of in-hospital bleedings requiring blood transfusion in patients with anaemia (3.2% vs. 0.5%; p < 0.001) as compared to these with normal Hb levels. Patients with anaemia more often required the use of intra-aortic balloon pump (IABP) (2.7% vs. 0.7%; p = 0.006) and had more cardiac arrests (1.3% vs. 0.2%; p = 0.020) during hospitalisation (Fig. 1).

#### Twelve-month outcome

One-year follow-up showed that there were higher rates of death in patients with anaemia in comparison to patients with normal Hb (p = 0.001; Fig. 2). The Kaplan-Meier analysis also revealed significantly better survival in patients with normal Hb in comparison to patients with anaemia (p = 0.001; Fig. 3). However, despite higher disease burden in patients with anaemia there was no difference in overall MACCE (composite death, MI, stroke, TVR) in comparison to patients with normal Hb (p = 0.096; Fig. 2). There was also no difference in death and MACCE in the population of patients with anaemia according to type of DES (I-DES vs. II-DES) (Fig. 4). The 12-month survival probability was presented using Kaplan-Meier curves stratified on I-DES vs. II-DES (Fig. 5). Multivariate Cox regression analysis revealed that independent risk factors of death among CAD and DES implanted were diabetes (HR = 1.674, 95% CI 1.01–2.76; p = 0.045), PAD (HR = 2.417, 95% CI 1.36-4.27; p = 0.002), LVEF < 50% (HR = 6.385, 95% CI 3.12-13.06; p < 0.001), and age > 65 years (HR = 2.802, 95% CI 1.57–4.98; p < 0.001) (Table 3).

#### **DISCUSSION**

Analysis of data obtained from the Katowice-Zabrze Registry, in regards to I-DES and II-DES revealed that high proportion of patients hospitalised with CAD treated with I-DES and II-DES also had anaemia. Anaemia was present in almost 11% of patients and frequently co-existed with advanced coronary artery stenosis.

#### Demographics, presentation, and comorbidities

Similar to the results observed in other studies, the population of patients with anaemia in this study consisted of older patients and included a higher percentage of advanced age [1, 4, 6, 10], diabetes [6, 10, 11], tachycardia [1, 10], longer hospital stay [6], lower body mass index [10], renal failure [12], and higher value of creatinine [10]. Furthermore, these patients more frequently have PAD, COPD, history of cardiovascular (CV) events, and revascularisation (PCI, CABG) [10]. These patients are less likely to have dyslipidaemia and family history of CAD compared with patients with normal Hb levels. On admission to hospital patients with acute MI and anaemia had higher Killip-Kimball class compared with patients with normal Hb levels, which corresponds with other studies, including a population of ACS patients enrolled in the meta-analysis by Sabatine et al. [1]. Similarly to the Maneveu et al. [13] study, we found higher risk of death according to the GRACE score in patients with anaemia.

#### Left ventricular ejection fraction

In current analysis only 48% patients with MI had normal LVEF, and moderate and severe LVEF dysfunction was significantly more frequent in patients with anaemia. The prognostic value

Table 1. Patients' characteristics, risk factors, and clinical presentation according to the presence of anaemia

|                                       | Anaemia (–)    | Anaemia (+)   | P       |
|---------------------------------------|----------------|---------------|---------|
|                                       | N = 1699 (89%) | N = 217 (11%) |         |
| Demographic data:                     |                |               |         |
| Age [years], median (IQR)             | 62 (56–70)     | 69 (61–75)    | < 0.001 |
| Male                                  | 1099 (64.6%)   | 137 (63.1%)   | 0.708   |
| Body mass index [kg/m²], median (IQR) | 29 (26–32)     | 27 (25–31)    | 0.038   |
| Discharge diagnosis:                  |                |               |         |
| Unstable angina                       | 1340 (78.8%)   | 160 (73.7%)   | 0.150   |
| NSTEMI                                | 245 (14.4%)    | 40 (18.4%)    | 0.118   |
| STEMI/LBBB                            | 116 (6.8%)     | 15 (6.9%)     | 0.960   |
| CAD history:                          |                |               |         |
| Previous MI                           | 790 (46.4%)    | 125 (57.6%)   | 0.002   |
| Previous PCI                          | 936 (55.0%)    | 128 (58.9%)   | 0.277   |
| Previous CABG                         | 330 (19.4%)    | 68 (31.3%)    | < 0.001 |
| CAD risk factors:                     |                |               |         |
| Hypertension                          | 1454 (85.5%)   | 189 (87.0%)   | 0.540   |
| Dyslipidaemia                         | 1143 (67.2%)   | 121 (55.7%)   | < 0.001 |
| Diabetes mellitus                     | 620 (36.4%)    | 97 (44.7%)    | 0.020   |
| Smoking                               | 424 (24.9%)    | 40 (18.4%)    | 0.283   |
| Family history                        | 572 (33.6%)    | 56 (25.8%)    | 0.020   |
| Concomitant disease:                  |                |               |         |
| Chronic obstructive pulmonary disease | 95 (5.5%)      | 22 (10.1%)    | 0.009   |
| Renal failure                         | 330 (19.4%)    | 68 (31.3)     | < 0.001 |
| Peripheral artery disease             | 92 (5.4%)      | 22 (10.1%)    | 0.005   |
| Left ventricular function:            |                |               |         |
| < 30%                                 | 139 (8.2%)     | 28 (12.9%)    | < 0.001 |
| 30–50%                                | 608 (35.8%)    | 98 (45.2%)    | < 0.001 |
| > 50%                                 | 952 (56%)      | 91 (41.9%)    | < 0.001 |
| Laboratory:                           |                |               |         |
| Hb [g/dL], median (IQR)               | 14.4 (13–15)   | 11.8 (11–12)  | < 0.001 |
| Creatinine [mg/dL], median (IQR)      | 0.8 (0.7–1.0)  | 0.9 (0.7–1.1) | < 0.001 |
| GFR [mL/min/1.73 m²], median (IQR)    | 83 (68–94)     | 72 (53–87)    | < 0.001 |
| Clinical status on admission:         |                |               |         |
| HR [bpm], median (IQR)                | 70 (60–78)     | 75 (65–80)    | 0.010   |
| SBP [mm Hg], median (IQR)             | 130 (120–150)  | 130 (120–145) | 0.301   |
| Canadian Cardiovascular Society:      |                |               | < 0.001 |
| I–II                                  | 556 (32.7%)    | 41 (18.9%)    |         |
| III–IV                                | 1143 (67.2%)   | 176 (81.1%)   |         |
| Killip class:                         |                |               | < 0.001 |
| I–II                                  | 354 (98.0%)    | 51 (92.7%)    |         |
| III–IV                                | 7 (1.9%)       | 4 (7.2%)      |         |
| GRACE score > 140                     | 192 (53.1%)    | 40 (72.7%)    | 0.010   |

IQR — interquartile range; NSTEMI — non-ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction; LBBB — left bundle branch block; CAD — coronary artery disease; MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery bypas grafting; Hb — haemoglobin on admission; GFR — glomerular filtration rate; HR — heart rate; SBP — systolic blood pressure

Table 2. Angiographic and procedural data

|   | Anaemia (–)    | Anaemia (+)   | Р       |  |
|---|----------------|---------------|---------|--|
|   | N = 1699 (89%) | N = 217 (11%) |         |  |
| SYNTAX score (points)                     | 14 (8–22)      | 21 (12–27)    | 0.001   |  |
| I-DES                                     | 571 (33.6%)    | 74 (34.1%)    | 0.005   |  |
| II-DES                                    | 1128 (66.4%)   | 143 (65.9%)   | 0.885   |  |
| No. of vessels with significant stenosis: |                |               | 0.001   |  |
| 1   | 655 (38.6%)    | 60 (27.6%)    |         |  |
| 2   | 601 (35.4%)    | 78 (35.9%)    |         |  |
| 3   | 443 (26.1%)    | 79 (36.4%)    |         |  |
| Type of the culprit lesion (AHA/ACC):     |                |               | < 0.001 |  |
| A   | 389 (23.7%)    | 37 (18.4%)    |         |  |
| В   | 995 (60.7%)    | 130 (64.7%)   |         |  |
| B/C                                       | 6 (0.4%)       | 6 (3.0%)      |         |  |
| С   | 250 (15.2%)    | 28 (13.9%)    |         |  |
| Target vessel:                            |                |               |         |  |
| Left main                                 | 197 (11.6%)    | 48 (22.1%)    | < 0.001 |  |
| Left anterior descending                  | 1373 (80.8%)   | 176 (81.1%)   | 0.918   |  |
| Left circumflex                           | 907 (53.4%)    | 143 (65.9%)   | < 0.001 |  |
| Right coronary artery                     | 907 (34.4%)    | 134 (61.8%)   | 0.020   |  |
| Arterial bypass graft                     | 76 (4.5%)      | 20 (9.2%)     | 0.002   |  |
| Saphenous vein graft                      | 177 (10.4%)    | 31 (14.3%)    | 0.085   |  |
| Average stent diameter [mm]               | 3 (2.5–3.5)    | 3 (2.5–3.5)   | 0.310   |  |
| Total stent length [mm]                   | 22 (15–28)     | 22 (15–28)    | 0.703   |  |

 $\hbox{I-DES} -\hbox{first-generation drug-eluting stents; II-DES} -\hbox{second-generation drug-eluting stents}$ 

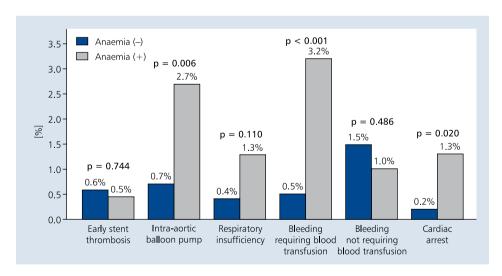


Figure 1. In-hospital adverse events

of anaemia in patients with STEMI and left ventricular dysfunction was documented in the TRACE study [5], which involved 1.731 patients with LVEF < 35%. Severe anaemia concomitant with a decrease in LVEF was associated with higher mortality, particularly in patients with heart failure.

#### **Bleeding**

Bleeding is the most frequent non-ischaemic complication observed in the management of non-ST-segment elevation acute coronary syndrome (NSTE-ACS), as well as in other clinical settings such as STEMI and PCI [14]. In the present

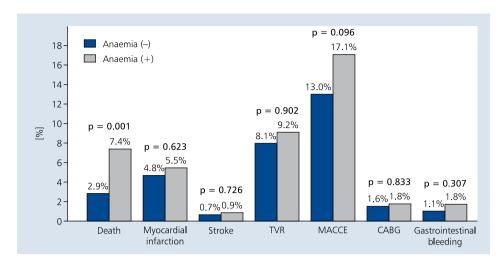


Figure 2. Incidence of major adverse cardiac and cerebrovascular events (MACCE) and bleeding events in 12-month follow-up; CABG — coronary artery bypas grafting; TVR — target vessel revascularisation

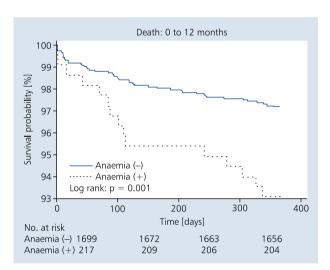


Figure 3. Kaplan-Meier survival curve in patients with and without anaemia

study there was increase risk of in-hospital bleeding requiring blood transfusion in patients with anaemia. Data from other studies showed a strong association between anaemia and increased risk of procedure-related as well as non-procedure-related bleeding in patients with ACS, including STEMI and NSTE-ACS, managed invasively. There was a gradual increase in the risk of bleeding and red blood cell transfusion, which was associated with an increased risk of CV events as Hb level decreased [10]. The ACUITY [15] major bleeding was associated with higher 30-day mortality, ischaemia, and stent thrombosis compared to patients without major bleeding, and was an independent predictor of 30-day mortality. In the Nikolsky et al. [16] study, patients with anaemia frequently developed in-hospital haemorrhagic complications (6.2% vs. 2.4%; p < 0.002) and had higher rates of blood product

transfusions (13.1% vs. 3.1%; p < 0.0001). Furthermore, Wu et al. [17] observed decreased 30-day mortality in ACS patients aged  $\geq$  65 years when a blood transfusion was performed at haematocrit  $\leq$  30%. Choosing the best vascular approach during PCI can significantly reduce the risk of bleeding. A radial approach reduced the incidence of blood transfusion by half and lowered the 30-day and one-year mortality [18]. The European Society of Cardiology (ESC) guidelines on diagnosis and treatment of NSTE-ACS recommended a blood transfusion in cases of compromised haemodynamic status or haematocrit < 25% or Hb level < 7 g/dL [14].

#### Interventional treatment

Interventional treatment in ACS is rarely practiced in patients with low Hb levels [10]. When selecting strategies, physicians should pay particular attention to the need for DAPT after PCI. However, despite the favourable results observed with the use of DAPT after PCI, for the prevention of stent thrombosis, DAPT is unfortunately also associated with an increased risk of major and minor bleeding compared to single-agent therapy [19]. Therefore, those patient need to individualised antiplatelet approach to decrease thrombotic events without increasing bleeding [20]. Another important issue is selection of the appropriate stent during PCI in patients with anaemia. According to the ESC guidelines, in patients with anaemia the use of DES should be restrictive due to the need for long-term DAPT [14]. Data from another study showed that PCI with II-DES is associated with lower risk of clinically meaningful restenosis, stent thrombosis, and a lower risk of death compared with I-DES [21]. Considering that the group of patients with anaemia have a higher risk of death [22], recurrent MI [2], and more common complex atherosclerotic lesions, they are at high risk of restenosis after PCI, which makes the use of DES particularly advantageous in them.

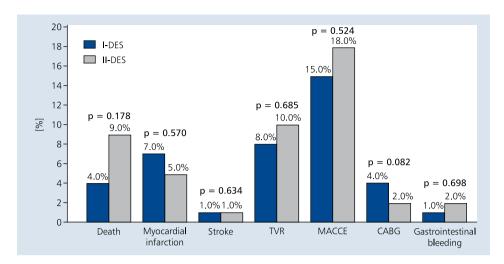


Figure 4. Incidence of major adverse cardiac and cerebrovascular events (MACCE) and bleeding events in 12-month follow-up. Comparison of first- (I-DES) vs. second-generation drug-eluting stent (II-DES) in patients with anaemia; CABG — coronary artery bypass grafting; TVR — target vessel revascularisation

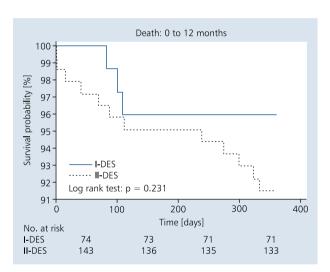


Figure 5. Kaplan-Meier survival curve in patients with anaemia treated with first- (I-DES) vs. second-generation drug-eluting stents (II-DES)

Table 3. Multivariate analysis Cox regression. All-cause mortality

|                                | P       | HR    | 95% CI     |
|--------------------------------|---------|-------|------------|
| Anaemia                        | 0.150   | 1.541 | 0.85-2.77  |
| Diabetes                       | 0.045   | 1.674 | 1.01-2.76  |
| Peripheral artery disease      | 0.002   | 2.417 | 1.36-4.27  |
| LVEF < 50%                     | < 0.001 | 6.385 | 3.12-13.06 |
| Age > 65 years                 | < 0.001 | 2.802 | 1.57-4.98  |
| Previous myocardial infarction | 0.571   | 1.163 | 0.69–1.95  |

HR — hazard ratio; CI — confidence interval; LVEF — left ventricular ejection fraction; MI — myocardial infarction

#### In-hospital outcome

In the current study, as in other studies, patients with anaemia during hospitalisation more often had sudden cardiac arrest [23] and indications for IABP [12] in comparison to patients with normal Hb levels. Moreover, patients with anaemia reported longer hospitalisation after PCI, which was also demonstrated by Lee et al. [6].

#### Twelve-month outcome

In 12-month follow-up mortality was significantly higher in CAD patients with anaemia. Several studies demonstrated the adverse effects of anaemia; however, a Hb threshold value that predicts possible adverse CV events would be most helpful in deciding on optimal intervention to improve outcome. Sabatine et al. [1] completed a meta-analysis of 16 clinical trials, which included a total of 39,922 patients. The goal was to assess the impact of anaemia on the occurrence of MACE in 30-day observation in order to identify a threshold value of Hb that increases the risk of adverse outcomes in ACS. This study showed that the relation between the risk of CV events and Hb levels has a reverse J-shaped distribution. It is noteworthy that the value of Hb below which there was an observed increase in MACE differed for STEMI and NSTEMI in the 30-day observation. In patients with STEMI, when Hb values of 14 g/dL to 15 g/dL were used as the reference, Hb levels below 14 g/dL were associated with an increase in mortality from CV causes for each 1 g/dL decrement in Hb. In patients with NSTEMI, when Hb values of 15 g/dL to 16 g/dL were used as the reference, Hb levels below 11 g/dL were associated with an increase in mortality from CV causes, MI, or recurrent ischaemia for each 1 g/dL decrement in Hb.

#### Limitations of the study

Patients were not randomised as to choice of stent implantation (I-DES or II-DES). There was no information on drugs used before admission to hospital, especially those with a known impact on the occurrence of anaemia (e.g. NSAIDs). There was no information about duration of medication (example patients taking clopidogrel) after PCI.

#### **CONCLUSIONS**

When CAD is coexistent with anaemia, it is associated with an increased risk of major in-hospital bleeding and acute heart failure, as well as mortality in one year follow-up. Incidence of anaemia in patients with CAD, who undergo PCI with DES is relatively high (approx. 11%), so Hb levels should be evaluated upon admission and considered in the risk stratification. There is no advantage of II-DES over I-DES in terms of MACCE and TVR in patients with anaemia.

#### Conflict of interest: none declared

#### References

- Sabatine MS, Morrow DA, Giugliano RP et al. Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. Circulation, 2005; 111: 2042–2049.
- Wojakowski W. Euro Heart Survey ACS III Registry (2006–2008) Presentd at ESC Congress 2009; 29 August – 02 September, 2009; Barcelona, Spain.
- Nikolsky E, Mehran R, Aymong ED et al. Impact of anemia on outcomes of patients undergoing percutaneous coronary interventions. Am J Cardiol, 2004; 94: 1023–1027. doi: 10.1016/j. amjcard.2004.06.058.
- Anker SD, Voors A, Okonko D 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: 1331–1339. doi: 10.1093/eurheartj/ehp116.
- Valeur N, Nielsen OW, McMurray JJ 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: 577–584. doi: 10.1016/j.ejheart.2005.11.017.
- Lee PC, Kini AS, Ahsan C et al. Anemia is an independent predictor of mortality after percutaneous coronary intervention. J Am Coll Cardiol, 2004; 44: 541–546. doi: 10.1016/j.jacc.2004.04.047.
- Shishehbor MH, Filby SJ, Chhatriwalla AK et al. Impact of drug-eluting versus bare-metal stents on mortality in patients with anemia. J Am Coll Cardiol Cardiovascular Interventions, 2008; 2: 329–336. doi: 10.1016/j.jcin.2008.11.014.
- Valgimigli M, Tebaldi M, Borghesi M et al. Two-year outcomes after first- or second-generation drug-eluting or bare-metal stent implantation in all-comer patients undergoing percutaneous coronary intervention: a pre-specified analysis from the PRODIGY study (PROlonging Dual Antiplatelet Treatment After Grading stent-induced Intimal hyperplasia study). J Am Coll Cardiol Cardiovascular Interventions, 2013; 7: 20–28. doi: 10.1016/j. jcin.2013.09.008.
- Nutritional anaemias. Report of a WHO scientific group. World Health Organization Technical Report Series, 1968; 405: 5–37.

- Bassand JP, Afzal R, Eikelboom J et al. Relationship between baseline haemoglobin and major bleeding complications in acute coronary syndromes. Eur Heart J, 2010; 31: 50–58. doi: 10.1093/eurheartj/ehp401
- Craig KJ, Williams JD, Riley SG, et al. Anemia and diabetes in the absence of nephropathy. Diabetes Care, 2005; 28: 1118–1123.
- NKF-DOQI clinical practice guidelines for the treatment of anemia of chronic renal failure. National Kidney Foundation-Dialysis
  Outcomes Quality Initiative. Am J Kid Dis, 1997; 30: S192–S240.
- Meneveau N, Schiele F, Seronde MF et al. Anemia for risk assessment of patients with acute coronary syndromes. Am J Cardiol, 2008; 103: 442-447. doi: 10.1016/j.amjcard.2008.10.023.
- 14. Hamm CW, Bassand JP, Agewall S et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the ESC. Eur Heart J, 2011; 32: 2999–3054. doi: 10.1093/eurheartj/ehr236.
- Manoukian SV, Feit F, Mehran R et al. Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY Trial. J Am Coll Cardiol, 2007; 49: 1362–1368. doi: 10.1016/j.jacc.2007.02.027.
- Nikolsky E, Aymong ED, Halkin A 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: 547–553. doi: 10.1016/j.jacc.2004.03.080.
- Wu WC, Rathore SS, Wang Y et al. Blood transfusion in elderly patients with acute myocardial infarction. New Engl J Med, 2001; 345: 1230–1236. doi: 10.1056/NEJMoa010615.
- Chase AJ, Fretz EB, Warburton WP et al. Association of the arterial access site at angioplasty with transfusion and mortality: the M.O.R.T.A.L study (Mortality benefit Of Reduced Transfusion after percutaneous coronary intervention via the Arm or Leg). Heart, 2007; 94: 1019–1025. doi: 10.1136/hrt.2007.136390.
- Serebruany VL, Malinin AI, Ferguson JJ et al. Bleeding risks of combination vs. single antiplatelet therapy: a meta-analysis of 18 randomized trials comprising 129,314 patients. Fundamental Clin Pharmacol, 2008; 22: 315–321. doi: 10.1111/j.1472-8206. 2008.00582.x.
- Winter MP, Koziński M, Kubica J et al. Personalized antiplatelet therapy with P2Y12 receptor inhibitors: benefits and pitfalls. Post Kardiol Interw, 2015; 11: 259–280. doi: 10.5114/pwki. 2015.55596.
- Sarno G, Lagerqvist B, Frobert O et al. Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Eur Heart J, 2012; 33: 606–613. doi: 10.1093/eurheartj/ehr479.
- Kruk M, Przyluski J, Kalinczuk L et al. Risk is not flat. Comprehensive approach to multidimensional risk management in ST-elevation myocardial infarction treated with primary angioplasty (ANIN STEMI Registry). Post Kardiol Interw, 2013; 9: 212–220. doi: 10.5114/pwki.2013.37498.
- McKechnie RS, Smith D, Montoye C et al. Prognostic implication of anemia on in-hospital outcomes after percutaneous coronary intervention. Circulation, 2004; 110: 271–277. doi: 10.1161/01. CIR.0000134964.01697.C7.

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# Znaczenie prognostyczne niedokrwistości u pacjentów z chorobą wieńcową leczonych metodą angioplastyki wieńcowej z wszczepieniem stentów uwalniających lek

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#### Streszczenie

**Wstęp:** Współwystępowanie niedokrwistości powoduje istotne zwiększenie ryzyka poważnych zdarzeń sercowo-mózgowo-naczyniowych (MACCE) oraz powikłań krwotocznych po przezskórnej interwencji wieńcowej (PCI), zwłaszcza w populacji pacjentów z ostrym zespołem wieńcowym.

**Cel:** Celem pracy było określenie wpływu niedokrwistości na częstość występowania MACCE u pacjentów leczonych PCI z implantacją stentu uwalniającego lek (DES) I i II generacji w obserwacji rocznej.

Metody i wyniki: Badaniem objęto grupę 1916 kolejnych pacjentów (UA: n = 1502; 78,3%; NSTEMI: n = 283; 14,7%; STEMI/LBBB: n = 131; 6,8%); leczonych pierwszą (34%) lub drugą (66%) generacją DES. Badaną populację podzielono na dwie grupy: pacjentów z niedokrwistością rozpoznaną przed PCI — 217 (11%) oraz osoby bez niedokrwistości — 1699 (89%). Przyjęto definicję niedokrwistości wg Światowej Organizacji Zdrowia (wartość hemoglobiny [Hb] < 13 g/dl dla mężczyzn i < 12 g/dl dla kobiet). Pacjenci z niedokrwistością byli starsi (69, IQR: 61–75 vs. 62, IQR: 56–70; p < 0,001), częściej współwystępowały u nich: cukrzyca (44,7% vs. 36,4%; p = 0.02), przewlekła choroba nerek (31,3% vs. 19,4%; p < 0.001), miażdżyca tętnic obwodowych (10,1% vs. 5,4%; p = 0,005) i upośledzona kurczliwość lewej komory (50, IQR: 40–57% vs. 55, IQR: 45–60%; p < 0,001). Nie wykazano różnicy w częstości występowania niedokrwistości w zależności od płci. Pacjenci z niedokrwistością częściej przebyli zawał serca (57,6% vs. 46,4%; p = 0,002) i zabieg pomostowania aortalno-wieńcowego (31,3% vs. 19,4%; p = 0,0001). U chorych tych cześciej obserwowano wielonaczyniowa chorobe wieńcowa (36% vs. 26%; p = 0,001) i bardziej nasilone zmiany miażdżycowe w skali SYNTAX (21, IQR: 12-27 pkt. vs. 14, IQR: 8-22 pkt.; p = 0,001). W obserwacji wewnątrzszpitalnej u pacjentów z niedokrwistością częściej dochodziło do rozwoju ostrej niewydolności serca (2,7% vs. 0,7%; p = 0,006) i krwawienia wymagającego transfuzji (3,2% vs. 0,5%; p < 0,001). Roczna obserwacja wykazała istotnie większe ryzyko zgonu u pacjentów z niedokrwistością, natomiast niedokrwistość pozostaje bez wpływu na częstość występowania zawału serca, ponownej angioplastyki w obrębie tego samego naczynia (TVR), udaru mózgu oraz MACCE. Nie stwierdzono różnic pod względem rodzaju wszczepianego stentu (I-DES vs. II-DES) u pacjentów z niedokrwistością.

**Wnioski:** U pacjentów z niedokrwistością występuje istotne większe ryzyko zgonu w obserwacji 12-miesięcznej, natomiast niedokrwistość pozostaje bez wpływu na częstość występowania zawału serca, ponownej rewaskularyzacji, udaru mózgu oraz MACCE. Nie ma przewagi II-DES nad I-DES w aspekcie MACCE oraz w częstości TVR u pacjentów z niedokrwistością.

Słowa kluczowe: przezskórna interwencja wieńcowa, stent uwalniający lek, niedokrwistość

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