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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Does admission anaemia still predict mortality six years after myocardial infarction?

Anna Tomaszuk-Kazberuk, Swietłana Bolińska, Elżbieta Młodawska, Paulina Łopatowska, Bożena Sobkowicz, Włodzimierz Musiał

Department of Cardiology, Medical University of Bialystok, Poland

Abstract

Background: Anaemia is present in 12–30% of patients with acute coronary syndromes (ACS). Many studies have shown that admission anaemia is an independent predictor of in-hospital or short-term mortality in patients with ACS. However, there is limited data on the long-term prognostic importance of anaemia in this group of patients.

Aim: To establish the relation between haemoglobin concentration on admission and six-year all-cause mortality in patients with ST-segment elevation myocardial infarction (STEMI) treated invasively.

Methods: We retrospectively studied 551 patients with the diagnosis of STEMI referred to the catheterisation laboratory of our hospital and treated with successful primary percutaneous coronary intervention. Patients were divided into two groups according to admission haemoglobin concentration (< 13 g/dL in males and < 12 g/dL in females).

Results: A total of 551 patients with STEMI (164 female, 30%) were included in the analysis, mean age was 63 ± 12 years. Anaemia on admission was present in 11% (n = 61) of the patients. Of the entire cohort, renal failure was present in 25% (n = 138), and diabetes in 16% (n = 88). Admission haemoglobin concentration was significantly associated with age ($r = –0.2663$, $p < 0.05$), blood pressure (systolic blood pressure [SBP]: $r = 0.1940$, diastolic blood pressure [DBP]: $r = 0.2023$, $p < 0.05$), glucose concentration ($r = –0.1218$, $p < 0.05$), white blood cells count ($r = 0.1230$, $p < 0.05$), cholesterol concentration ($r = 0.1253$, $p < 0.05$), estimated glomerular filtration rate (eGFR; $r = 0.1819$, $p < 0.05$), Killip-Kimball class ($r = –0.1387$, $p < 0.05$) and TIMI risk score for STEMI ($r = –0.2647$, $p < 0.05$). During follow-up, 27% (n = 130) of the patients died. The mortality rate was significantly higher in the patients with admission anaemia (47% vs. 24%, $p = 0.0002$). The patients with anaemia were older ($p = 0.0007$), had lower blood pressure (SBP: $p = 0.007$; DBP: $p = 0.01$), higher heart rate ($p = 0.03$), higher glycaemia concentration ($p = 0.003$), higher C-reactive protein concentration ($p = 0.0007$) and lower white blood cells count ($p = 0.03$). Patients with anaemia had more frequently renal failure (eGFR < 60 mL/min/1.73 m^2) ($p = 0.02$) and a significantly higher TIMI risk score for STEMI ($p = 0.01$). In multivariate analysis, all-cause mortality was associated with: anaemia on admission (OR = 2.29; 95% CI 1.20–4.36; $p = 0.011$), low ejection fraction (OR = 2.97; 95% CI 1.78–4.96; $p < 0.001$) and age (OR = 1.65 [per 10 years]; 95% CI 1.34–2.03; $p < 0.001$). Anaemia on admission remained an independent predictor of six-year mortality.

Conclusions: Admission anaemia significantly influences all-cause mortality in patients with STEMI treated invasively in a six-year follow-up and may be used for risk stratification in this population.

Key words: anaemia, ST-elevated myocardial infarction, mortality

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INTRODUCTION

Anaemia is common in patients admitted to cardiac intensive care units, and is present in 12–30% of patients with acute coronary syndromes (ACS) [1, 2]. Many studies have shown that admission anaemia is an independent predictor of in-hospital or short-term mortality in patients with ACS [3, 4]. However, there is limited data on the long-term prognostic importance of anaemia in this group of patients. The aim of our study was to establish the relation between haemoglobin concentration and six-year all-cause mortality in patients with ST-segment elevation myocardial infarction (STEMI) treated invasively.

Address for correspondence:
Anna Tomaszuk-Kazberuk, MD, PhD, Department of Cardiology, Medical University of Bialystok, ul. M. Skłodowskiej-Curie 24A, 15–276 Białystok, Poland, tel: +48 85 7468 656, fax: +48 85 7468 604, e-mail: walkaz@poczta.fm

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METHODS

Study population

We retrospectively studied 551 patients with the diagnosis of STEMI referred to the catheterisation laboratory of our hospital and treated with successful primary percutaneous coronary intervention (PCI) in 2005. An ACS was diagnosed and treated using current guidelines [5]. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the local ethics committee. Upon joining the study, medical history was recorded, and all patients underwent physical examination, resting electrocardiogram (ECG), routine transthoracic echocardiography and coronary angiography. Patients were divided into two groups according to admission haemoglobin concentration.

Definitions

STEMI was defined as the presence of typical clinical presentation, an ST-elevation on ECG in two adjacent leads, > 0.2 mV for precordial leads and 0.1 for the remaining leads and elevated levels of myocardial injury markers (the creatinine kinase MB fraction [CK-MB]) [5].

Anaemia, based on World Health Organisation (WHO) criteria, was defined as baseline haemoglobin concentration < 13 g/dL in males and < 12 g/dL in females [6].

Echocardiographic analysis

Left ventricular ejection fraction (LVEF) was assessed in transthoracic echocardiography using the modified biplane Simpson's method (Philips Ultrasound System Sonos 5500, equipped for harmonic imaging with a 3.6 MHz transducer) and was derived in accordance with the recommendations of the European Society of Echocardiography [7].

Primary angioplasty

All patients underwent cardiac catheterisation and intervention by standard Judkins techniques. Luminal stenosis more than 75% by diameter was regarded as significant (visual assessment). The infarct related artery was identified based on coronary anatomy, ECG changes and regional left ventricular dysfunction. The PCI procedure was considered to be successful when the residual stenosis was less than 30% in the absence of dissection and thrombosis.

Follow-up

The primary end-point was all-cause mortality in a six-year follow-up. All data was obtained from the Polish population registry in Bialystok (Podlasie Voivodship Office) or telephone contact with the patients.

Statistical analysis

Distribution of every variable was tested with Kolmogorov-Smirnov test. Afterwards, the Student's t test or the Mann-Whitney U test was used for statistical analysis where applicable. Additional analysis of correlations between non-categorical variables was performed using Spearman tests. We carried out the multiple logistic regression model. Survival rates were displayed with Kaplan-Meier curves. Data is expressed as means and standard deviations. A p value of less than 0.05 was considered as statistically significant. The statistical software StatSoft, STATISTICA (data analysis software system) version 10, was used.

RESULTS

Baseline characteristics

A total of 551 patients with STEMI (164 female, 30%) were included in the analysis, mean age was 63 ± 12 years. Anaemia on admission was present in 11% (n = 61) of the patients. Clinical and laboratory characteristics of the study population are presented in Table 1. Admission haemoglobin concentration was significantly associated with age ($r = –0.2663$, $p < 0.05$), blood pressure (systolic blood pressure [SBP]: $r = 0.1940$, diastolic blood pressure [DBP]: $r = 0.2023$, $p < 0.05$), concentration of glucose ($r = –0.1218$, $p < 0.05$), white blood cells (WBC) count ($r = 0.1230$, $p < 0.05$), cholesterol concentration ($r = 0.1253$, $p < 0.05$), estimated glomerular filtration rate (eGFR; $r = 0.1819$, $p < 0.05$), Killip-Kimball class ($r = –0.1387$, $p < 0.05$) and TIMI risk score for STEMI ($r = –0.2647$, $p < 0.05$).

During follow-up, 27% (n = 130) of the patients died. They were significantly older ($p < 0.001$), had higher admission glycaemia and CK-MB concentration ($p < 0.001$, $p = 0.04$, respectively), and lower eGFR and LVEF ($p = 0.00008$, $p < 0.001$, respectively).

In multivariate logistic regression analysis, all-cause mortality was associated with: anaemia on admission (OR = 2.29, 95% CI 1.20–4.36, p = 0.011), low LVEF (OR = 2.97, 95% CI 1.78–4.96, $p < 0.001$) and age (OR = 1.65 [per 10 years], 95% CI 1.34–2.03, $p < 0.001$). eGFR < 60 mL/min/1.73 m^2 was also included in the analysis but it did not correlate with mortality. Anaemia on admission remained an independent predictor of six-year mortality.

Characteristics of the group with admission anaemia

The mortality rate was significantly higher in patients with admission anaemia (47% vs. 24%, $p = 0.0002$). The Kaplan-Meier survival curves according to the admission anaemia are shown in Figure 1.

Clinical and laboratory characteristics of the patients with and without anaemia are presented in Table 2. Patients with admission anaemia were significantly older, had significantly lower blood pressure, higher heart rate, higher glycaemia concentration, higher C-reactive protein (CRP) concentration and lower WBC count. Renal failure was more frequently observed in anaemic patients. The two groups did not differ in terms of medical history, LVEF and infarction location. The

Table 1. Clinical and laboratory characteristics of the population

Male	386 (70%)
Age [years]	63.49 ± 11.93
Prior PCI	30 (6%)
Prior CABG	10 (2%)
Prior stroke	37 (7%)
Prior MI	64 (12%)
Smoker	231 (50%)
Diabetes mellitus	88 (16%)
Ejection fraction [%]	45.17 ± 9.75
Killip class	2.31 ± 6.11
TIMI score for STEMI	3.68 ± 4.73
Systolic BP [mm Hg]	136 ± 28
Diastolic BP [mm Hg]	85 ± 17
Heart rate [bpm]	77 ± 19
CK on admission [IU]	519.85 ± 889.54
CK max. [IU]	2,066.75 ± 2,044.51
CK-MB on admission [IU]	68.73 ± 82.11
CK-MB max. [IU]	243.20 ± 381.18
Glucose [mg/dL]	114.26 ± 33.27
Glucose > 140 mg/dL	76 (15%)
Serum creatinine [mg/dL]	1.28 ± 4.79
eGFR [mL/min/1.73 m^2]	76.17 ± 27.68
eGFR < 60 mL/min/1.73 m^2	138 (25%)
CRP [mg/L]	36.60 ± 56.97
CRP > 10 mg/L	318 (68%)
WBC count [G/L]	11.70 ± 3.63
WBC count > 10 G/L	352 (64%)
Haemoglobin [g/dL]	14.15 ± 1.42
Infarct related artery:	
Left anterior descending	231(42%)
Right coronary	226 (41%)
Marginal branches	11 (2%)
Circumflex	55 (10%)
Intermedial	6 (1%)
Posterolateral branch	6 (1%)
Follow-up [days]	2,153.90 ± 1,931.30
Mortality	130 (27%)

PCI — elective percutaneous coronary intervention; CABG — coronary artery bypass graft; MI — myocardial infarction; STEMI — ST-segment elevation myocardial infarction; BP — blood pressure; CK — creatine kinase; CK-MB — creatine kinase-MB fraction; eGFR — estimated glomerular filtration rate; CRP — C-reactive protein; WBC — white blood cells

anaemic patients had significantly higher TIMI risk score for STEMI and the rate of in-hospital cardiovascular complications was twice that in non-anaemic patients.

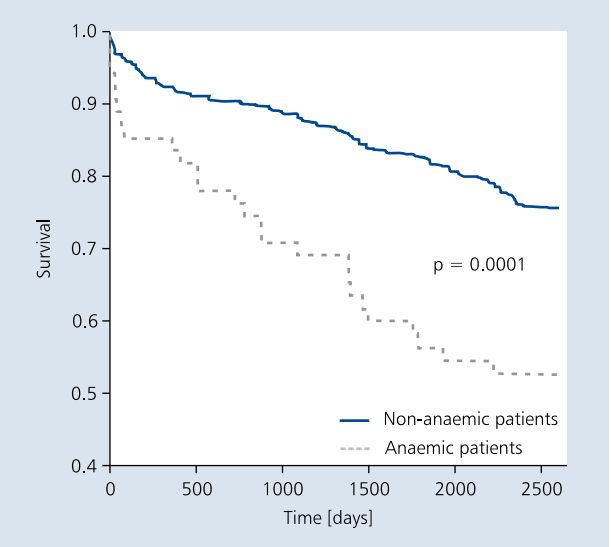

Figure 1. Kaplan-Meier survival curve according to admission anaemia

Women with admission anaemia had more frequently glycaemia concentration > 140 mg/dL (45% vs. 17%, p = 0.002), higher CRP concentration (56 vs. 25 mg/L, p = 0.009) and WBC count within the limits of normality (36% vs. 61%, p = 0.002). The anaemic women had significantly higher TIMI risk score for STEMI (6 vs. 4, p = 0.003). Admission anaemia in women did not correlate with all-cause mortality (43% vs. 29%, p = 0.19).

Men with admission anaemia were significantly older (67 vs. 60 years, p = 0.002), had significantly lower blood pressure (SBP: 123 vs. 137 mm Hg, p = 0.002; DBP: 77 vs. 85 mm Hg, p = 0.002), higher CRP concentration (75 vs. 36 mg/L, p = 0.0008) and WBC count within the limits of normality (49% vs. 68%, p = 0.02). The mortality rate was significantly higher in men with admission anaemia (50% vs. 21%, p = 0.0002).

DISCUSSION

In this study, we found that admission anaemia in patients with STEMI significantly correlates with all-cause mortality in a six-year follow-up.

Patients with myocardial infarction (MI) and anaemia have a high risk profile with coexisting diabetes, hypertension and renal failure [8]. Several studies have shown that anaemia in patients with chronic heart failure is related to higher rate of hospitalisation, worse clinical condition on admission (higher Killip class) and rapid deterioration of renal function [9]. Furthermore, admission anaemia in MI is associated with higher in-hospital, short-term and one-year mortality [10, 11].

A reduction of 1 g/dL haemoglobin concentration is associated with a 13% increased risk for death and hospital

Table 2. Clinical and laboratory characteristics of the patients with and without anaemia

	Non-anaemic patients	Anaemic patients	p
Male	71%	64%	NS
Age [years]	62.92 ± 11.82	68.36 ± 11.11	0.001
Prior PCI	6%	8%	0.497
Prior CABG	2%	0%	NS
Prior stroke	7%	6%	NS
Prior myocardial infarction	12%	18%	NS
Smoker	51%	42%	NS
Diabetes mellitus	15%	21%	NS
Ejection fraction [%]	45.45 ± 9.75	43.41 ± 9.21	NS
TIMI score for STEMI	3.49 ± 4.92	5.14 ± 2.38	0.012
Systolic blood pressure [mm Hg]	137.31 ± 27.41	127.13 ± 28.55	0.007
Diastolic blood pressure [mm Hg]	85.46 ± 17.01	79.69 ± 19.37	0.014
Heart rate [bpm]	76.72 ± 18.73	82.45 ± 21.87	0.029
CK on admission [IU]	504.37 ± 861.56	654.34 ± 1,097.52	NS
CK max. [IU]	2,109.28 ± 2,102.4	1,721.58 ± 1,455.29	NS
CK-MB on admission [IU]	67.49 ± 78.33	80.10 ± 108.61	NS
CK-MB max. [IU]	248.35 ± 397.47	202.16 ± 195.99	NS
Glucose concentration [mg/dL]	112.91 ± 31.72	125.45 ± 42.75	0.008
Glucose > 140 mg/dL	14%	29%	0.003
Serum creatinine concentration [mg/dL]	1.28 ± 5.08	1.25 ± 0.63	NS
eGFR (mL/min/1.73 m^2)	77.00 ± 26.92	69.43 ± 32.80	0.044
eGFR < 60 mL/min/1.73 m^2	24%	38%	0.016
C-reactive protein concentration [mg/L]	33.04 ± 51.15	66.99 ± 88.00	0.000
C-reactive protein > 10 mg/L	66%	84%	0.014
White blood cells count [G/L]	11.80 ± 3.51	10.75 ± 4.37	0.034
White blood cells count > 10 G/L	66%	44%	0,001
Red blood cells count [G/L]	4.69 ± 0.44	3.84 ± 0.46	< 0.001
Haemoglobin concentration [g/dL]	14.45 ± 1.17	11.80 ± 0.99	< 0.001
Infarct related artery:			
Left anterior descending	42%	48%	NS
Right coronary	42%	39%	NS
Marginal branches	2%	2%	NS
Circumflex	11%	7%	NS
Intermedial	1%	0%	NS
Posterolateral branch	0%	2%	NS
Follow-up [days]	2,216.60 ± 2,016.7	1,695.45 ± 973.39	NS
Mortality	24 %	47%	0.0002

PCI — elective percutaneous coronary intervention; CABG — coronary artery bypass graft; STEMI — ST-segment elevation myocardial infarction; CK — creatine kinase; CK-MB — creatine kinase-MB fraction; eGFR — estimated glomerular filtration rate; NS — non-significant

readmission, and a reduction of 0.5 g/dL is associated with a 32% increased risk for left ventricular hypertrophy [12]. The underlying mechanism of increased rate of mortality in anaemic patients remains unclear. It might be associated with increased sympathetic tonus, tendency to bleed [13, 14], the severity of myocardial ischaemia [15] and more frequent occurrence of cardiogenic shock [16].

The effect of admission anaemia on the appearance and course of ACS is still intensively studied. According to various sources, the incidence of anaemia in ACS ranges from 12% to

30% [1, 2]. This discrepancy may be due to the heterogeneity of the studied populations. Most of the studies refer to all forms of ACS and various therapeutic procedures. Data regarding anaemia in patients with STEMI is limited and refers to in-hospital and short-term mortality [17]. Our study is the first to have shown the prognostic value of admission anaemia in a six-year follow-up.

In Tsujita's et al. study [18] involving 3,153 STEMI patients, anaemia was an independent predictor of reinfarction, bleeding and one-year mortality. The long-term prognostic significance of anaemia was investigated by Valeur et al. [2] in 1,731 both STEMI and non-STEMI patients. The authors reported that anaemia was an independent predictor of mortality in patients with acute MI and left ventricular systolic dysfunction, but the prognostic importance of anaemia was confined to the first year following acute MI. The increased risk was driven by patients with severe anaemia and heart failure.

The advantage of our study is that we analysed a homogenous group of patients exclusively diagnosed with STEMI.

The use of different cut-off points for haemoglobin concentration affects the rate of diagnosed anaemia and its prognostic value. In most of the studies, anaemia is defined according to the WHO definition (haemoglobin concentration < 12 g/dL in women and < 13 g/dL in men) [6]. We decided to use this popular definition of anaemia in our study. However, in some analysis, these values for haemoglobin showed no prognostic significance in ACS patients. Valeur et al. [2] found that lower haemoglobin concentration, < 10 g/dL in women and < 11 g/dL in men, was associated with increased mortality in acute MI patients. Sabatine et al. [3] showed that not only low but also high haemoglobin concentration is associated with an increased risk of death, and that these values differ depending on the type of ACS (in STEMI > 17 g/dL and < 14 g/L, in non-STEMI > 16 g/dL and < 11 g/dL). Go et al. [19] showed that very high (≥ 17 g/dL) or reduced (< 13 g/dL) haemoglobin concentration and chronic kidney disease independently increase the risk of death and hospitalisation in patients with heart failure, regardless of the systolic function. In our study, the lower limit of normal according to the WHO turned out to correlate with long term prognosis in patients with STEMI.

Limitations of the study

Unfortunately we were not able to obtain data on the rate of cardiovascular death, adverse cardiovascular events or the rate of stent thrombosis.

CONCLUSIONS

Admission anaemia significantly influences all-cause mortality in patients with STEMI treated invasively in a six-year follow-up and may be used for risk stratification in this population.

Conflict of interest: *none declared*

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Czy niedokrwistość przy przyjęciu do szpitala wpływa na śmiertelność po 6 latach od wystąpienia zawału serca?

Anna Tomaszuk-Kazberuk, Swietłana Bolińska, Elżbieta Młodawska, Paulina Łopatowska, Bożena Sobkowicz, Włodzimierz Musiał

Klinika Kardiologii, Uniwersytet Medyczny w Białymstoku, Białystok

Streszczenie

Wstęp: Niedokrwistość jest często diagnozowana u pacjentów hospitalizowanych na oddziałach intensywnej opieki kardiologicznej. Występuje u 12–30% chorych z ostrymi zespołami wieńcowymi. W wielu badaniach wykazano, że niedokrwistość przy przyjęciu do szpitala jest niezależnym predyktorem śmiertelności wewnątrzszpitalnej i krótkoterminowej. Jednak dane dotyczące wpływu niedokrwistości na śmiertelność długoterminową są ograniczone, a wnioski nie są jednoznaczne.

Cel: Celem badania było ustalenie związku między stężeniem hemoglobiny przy przyjęciu do szpitala a śmiertelnością całkowitą u pacjentów z zawałem serca z uniesieniem odcinka ST (STEMI) leczonych inwazyjnie za pomocą pierwotnej plastyki wieńcowej w obserwacji 6-letniej.

Metody: Retrospektywną analizą objęto 551 osób ze STEMI przyjmowanych w celu wykonania pierwotnej plastyki wieńcowej w ciągu 12 h od początku wystąpienia bólu zawałowego. Chorzy byli podzieleni na dwie grupy w zależności od stężenia hemoglobiny przy przyjęciu (< 13 g/dl u mężczyzn i < 12 g/dl u kobiet). Zastosowano definicję niedokrwistości wg Światowej Organizacji Zdrowia.

Wyniki: Spośród 551 pacjentów ze STEMI 30% stanowiły kobiety (n = 164), średni wiek wynosił 63 ± 12 lat. Niedokrwistość przy przyjęciu występowała u 11% (n = 61) osób. Przewlekłą chorobę nerek stwierdzono u 25% (n = 138), cukrzycę u 16% (n = 88) chorych. Stężenie hemoglobiny przy przyjęciu korelowało istotnie statystycznie z wiekiem (r = –0,2663; p < 0,05), wartością ciśnienia tętniczego (skurczowe ciśnienie tętnicze [SBP]: r = 0,1940, rozkurczowe ciśnienie tętnicze [DBP]: r = 0,2023; p < 0,05), stężeniem glukozy (r = –0,1218; p < 0,05), liczbą białych krwinek (r = 0,1230; p < 0,05), stężeniem cholesterolu całkowitego (r = 0,1253; p < 0,05), wartością szacowanej filtracji kłębuszkowej (eGFR; r = 0,1819; p < 0,05), klasą Killipa-Kimballa (r = –0,1387; p < 0,05) i skalą ryzyka TIMI dla STEMI (r = –0,2647; p < 0,05). Podczas obserwacji zmarło 27% (n = 130) pacjentów. Śmiertelność całkowita była istotnie wyższa w grupie chorych z niedokrwistością przy przyjęciu (47% vs. 24%; p = 0,0002). Chorzy z niedokrwistością byli starsi (p = 0,0007), charakteryzowali się niższymi wartościami ciśnienia tętniczego (SBP: p = 0,007; DBP: p = 0,01), szybszym rytmem serca (p = 0,03), wyższym stężeniem glukozy (p = 0,003), wyższym stężeniem białka C-reaktywnego (p = 0,0007) oraz niższą liczbą białych krwinek (p = 0,03). Przewlekłą chorobę nerek (eGFR < 60 ml/min/1,73 m^2) częściej obserwowano u pacjentów z niedokrwistością (p = 0,02). Obie grupy nie różniły się, jeśli chodzi o wywiad, frakcję wyrzutową lewej komory (LVEF) i lokalizację zawału serca. Pacjenci z niedokrwistością mieli więcej punktów w skali ryzyka TIMI dla STEMI (p = 0,01). W analizie wieloczynnikowej wykazano, że niezależnymi czynnikami ryzyka zgonu były: niedokrwistość przy przyjęciu (OR = 2,29; 95% CI 1,20–4,36; p = 0,011), niska LVEF (OR = 2,97; 95% CI 1,78–4,96; p < 0,001) i wiek chorych (na każde 10 lat OR = 1,65; 95% CI 1,34–2,03; p < 0,001). Niedokrwistość stwierdzana przy przyjęciu pozostawała niezależnym predyktorem 6-letniej śmiertelności.

Wnioski: Niedokrwistość przy przyjęciu do szpitala jest jednym z istotnych czynników wpływających na śmiertelność całkowitą u pacjentów ze STEMI leczonych inwazyjnie w obserwacji długoterminowej i może być użyta w stratyfikacji ryzyka w tej populacji.

Słowa kluczowe: niedokrwistość, zawał serca z uniesieniem odcinka ST, śmiertelność

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Adres do korespondencji:
dr hab. n. med. Anna Tomaszuk-Kazberuk, Klinika Kardiologii, Uniwersytet Medyczny w Białymstoku, ul. M. Skłodowskiej-Curie 24A, 15–276 Białystok, tel: +48 85 7468 656, faks + 48 85 7468 604, e-mail: walkaz@poczta.fm
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