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Acetylsalicylic acid resistance risk factors in patients with myocardial infarction

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ABSTRACT

Background: Despite its commonly recognized benefits in the cardiovascular disease setting, an issue of resistance to this drug has lately emerged. The aim of this research was assessment of the phenomenon of acetylsalicylic acid (ASA) resistance and its risk factors in patients treated for myocardial infarction.
Methods: This study is a *post-hoc* analysis of a previous prospective study with approximately 200 patients treated for myocardial infarction with a coated formulation of ASA. The population was divided into two subgroups according to the response to ASA.

ASA responsiveness was assessed using the arachidonic acid-dependent platelet aggregation (ASPI-test). The measurements were performed using the technique of impedance aggregometry.
Results: The prevalence of aspirin resistance among the study population was 6.2%. All analyzed aggregometric parameters (including ASPI-test, adenosine diphosphate dependent platelet aggregation – ADP-test, bleeding time measurement) showed significant differences between both subgroups. ASA resistant patients had higher concentrations of brain natriuretic peptide (BNP), high-sensitivity C-reactive protein (hs-CRP), leukocytes (WBC) and platelets (PLT) but lower concentrations of hemoglobin (HGB). The temporal point analysis for both subgroups showed aspirin resistance incidence peak in patients at 9 months after myocardial infarction.
Conclusions: The prevalence of aspirin resistance in our study population is comparable with rates reported in literature among patients with cardiovascular diseases. There is a possible relation between aspirin resistance and clopidogrel resistance. Presence did not affect the incidence of the clinical end-points.

Background

Cardiovascular system diseases inducted by atherosclerosis-based changes are currently major death cause in all over the world [1]. Platelets play a crucial role in pathophysiology of thrombotic atherosclerosis complications and therefore antiplatelet therapy underlies the treatment of these diseases as well as secondary prevention [2–4].

Acetylsalicylic acid (ASA) resistance is a new and very well documented phenomenon. Data on the spread of aspirin resistant varies greatly (from 0.4 to 83%) and depends on the laboratory method used [5–9]. Particular attention must be paid for relation between aspirin resistance risk factors that are also ischemic disease risk factors [10]. Evaluation of the platelets reactivity itself in patients taking aspirin helps to estimate effectiveness of treatment and modification in patients weakly responding to pharmacotherapy [11].

Platelet function tests are common in the assessment of bleeding and thrombosis risk as well as in effectively run antiplatelet drug therapy monitoring [12,13]. However, there is no standardized method to assess thrombocyte function and to

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Table 1
Clinical and demographic characteristics, risk factors, characteristic of angiographic image and performed percutaneous transluminal coronary angioplasty in study population [median (lower quartile – upper quartile) or number (percent)].

Study feature	Property value ($n = 194$)
Age [years]	60.5 (53.0–67.0)
Height [cm]	170.0 (164.0–176.0)
Body mass [kg]	80.0 (70.0–90.0)
Girth [cm]	96.0 (89.5–103.5)
Sex [men/women]	144/50
Ischemic disease recognized before admittance	48 (24.7%)
Infarction passed before admittance	19 (9.8%)
PTCA passed before admittance	13 (6.7%)
CABG passed before admittance	5 (2.6%)
Heart failure recognized before admittance	13 (6.7%)
Final diagnosis	
NSTEMI/UA	27 (14%)
STEMI	167 (86%) including: Anterior myocardial infarction 58 (29.9%) Inferior myocardial infarction 85 (43.8%) Other localization 24 (12.3%)
Risk factors for ischemic heart disease	
BMI [kg/m^2]	27.6 (24.9–30.7)
Hyperlipidemia in interview	124 (63.9%)
Hypertension	108 (55.7%)
Diabetes	68 (35.05%) (including 46 patients with newly recognized diabetes)
Current smokers	102 (52.58%)
Past smokers	39 (20.1%)
Positive family interview	52 (26.8%)
Lipid profile	
Total cholesterol [mg/dl]	214.0 (179.0–241.0)
LDL cholesterol [mg/dl]	140 (115.0–170.0)
HDL cholesterol [mg/dl]	40.0 (34.0–47.0)
Triglycerides [mg/dl]	104.5 (71.0–155.0)
Number of risk factors for IHD[a]	
1	3 (1.55%)
2	12 (6.18%)
3	34 (17.52%)
4	68 (35.0%)
5	44 (22.68%)
6	29 (14.95%)
7	4 (2.06%)
Other	
Glycaemia at admittance [mmol/L]	7.6 (6.5–8.9)
HbA1C [%]	6.0 (5.8–6.4)
Arachidonic acid-dependent aggregation [U]	13.0 (7.0–20.0)
ADP-dependent aggregation [U]	25.0 (17.0–37.0)
Bleeding time [min]	5.0 (4.0–6.5)
WBC [10^9 L^{-1}]	7.79 (6.56–9.19)
RBC [10^{12} L^{-1}]	4.5 (4.2–4.82)
HGB [g/L]	135 (128–144)
HCT [L/L]	0.39 (0.37–0.42)
PLT [10^9 L^{-1}]	208.0 (177.0–242.0)
MPV [fL]	10.9 (10.3–11.4)
BNP [pg/ml]	118.65 (64.6–228.6)
hs-CRP [mg/L]	12.2 (4.9–32.0)
LVEF [%]	45 (40.0–50.0)
Number of crucially narrowed vessels	
One vessel disease	80 (41.2%)
Two vessel disease	50 (25.8%)
Three vessel disease	64 (33.0%)
Outgoing blood flow	
TIMI 0	83 (42.8%)
TIMI 1	18 (9.3%)
TIMI 2	21 (10.8%)
TIMI 3	72 (37.0%)

evaluate cut-off values widely accepted to classify patient to the group of "resisted" or "responsive" to ASA activity currently. There are no counter indications against running basic test toward antiplatelet treatment resistance in daily clinical practice and to chronic monitoring of antiplatelet treatment effects. Trials to individualize treatment for the patients in reasonable cases (e.g. thrombosis in stent) can be made but only in clinical centers with proper experience [14].

According to available literature there is strict connection between fatal cardiovascular events and ineffective inhibition of thrombocyte activity by ASA, that is known as ASA resistance. Patients with confirmed ASA resistance have four times higher risk of fatal cardiovascular events appearance during the ASA therapy than the patient reacting to the treatment correctly [15].

Risk factors for incorrect aspirin response are thought to be: female sex, older age, obesity, nicotinism, diabetes, hypertension, heart failure, hypercholesterolemia, physical effort, acute coronary syndromes, state after coronary artery bypass surgery treatment, state after coronary angioplasty [16].

The aim of the study was to identify the risk factors of ASA resistance and evaluate the occurrence of aspirin resistance phenomenon during hospitalization and during follow-up visits in patients with myocardial infarction.

Materials and study methods

This study was designed as *post-hoc* prospective research analysis and comprised of patients hospitalized in Department of

Table 1 (*Continued*)

Study feature	Property value ($n = 194$)
End blood flow	
TIMI 1	1 (0.5%)
TIMI 2	5 (2.6%)
TIMI 3	188 (97%)
Number of implanted stents	
1	136 (70.1%)
2	40 (20.6%)
3	13 (6.7%)
4	4 (2.06%)
5	0 (0.00%)
6	1 (0.5%)
Total stents length [mm]	24.0 (15.0–31.5)
Average stents diameter [mm]	3.25 (2.87–3.5)
Revascularization	
Total	115 (59.3%)
Partial	79 (40.7%)
Qualification for further treatment:	
Conservative	153 (78.9%)
PTCA	30 (15.5%)
CABG	11 (5.7%)
Coronary artery change character	
De novo	176 (90.7%)
Restenosis	12 (6.2%)
Thrombosis	6 (3.0%)

ASA, acetylsalicylic acid; PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; UA, unstable angina; BMI, body mass index; LDL, low density lipoproteins; HDL, high density lipoproteins; HbA1c, glycated hemoglobin; ADP, adenosine diphosphate; WBC, white blood cells; RBC, red blood cells; HGB, hemoglobin; Hct, hematocrit; PLT, platelets; MPV, mean platelet volume; BNP, brain natriuretic peptide; hs-CRP, high sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; TIMI, thrombolysis in myocardial infarction; IHD, ischemic heart disease.

[a] Risk factors for ischemic heart disease: positive family interview, hypertension, diabetes, current nicotinism, LDL > 115 mg/dl, age >65 years old, BMI > 25 kg/m^2.