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# Single nucleotide polymorphisms may be useful as short-term predictors after coronary artery by-pass grafting surgery: the role of *FGB* g.4884C>T polymorphism

## Oznaczanie polimorfizmów genowych może być przydatne w ocenie krótkoterminowego ryzyka okołooperacyjnego po zabiegach pomostowania aortalno-wieńcowego: rola polimorfizmu *FGB* g.4884C>T

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We read with great interest the paper by Rywik et al. [1] on the application and utility of complex polymorphism analysis in the assessment and prognosis after percutaneous coronary intervention.

The authors observed that despite non-significant differences in the gene variants distribution between patients and controls, only E-selectine gene variants (SELE Ser128Arg) could be useful for patient stratification.

The previously reported gene variant SELE S128R is a synonym for S149R (rs5361), a single nucleotide polymorphism (SNP) based on NCBI Reference Sequence, Accession No: NM_000450.2. In the literature, both names are used. However, according to the standard system for naming human genes, we recommend using *ESELE* c.445A>C notation [2].

This common SNP of the E-selectin gene is a missense exchange of A to C nucleotides, resulting in the substitution of arginine (R) for serine (S) at position 149 (S149R) within the epidermal growth factor-like domain of the mature protein [3]. This arginine substitution causes the loss of E-selectin protein requirement for alpha 1-3-linked fucose to specific ligand binding. Additionally, the 149R phenotype alters E-selectin binding to heparin or sulfatide [4]. Clinical trials have revealed that the 149R allele is associated with the early onset of severe coronary artery disease (CAD) in subjects under 50 years of age, the presence of coronary artery calcification, and the increased risk of restenosis after percutaneous transluminal angioplasty in patients with peripheral artery disease [5–7].

In our study which was recently published the endothelium-leukocyte interaction is enhanced by genetic modification and results in the elevation of coagulation factors and platelet mediators ($\beta$-thromboglobulin) [8]. This enhanced endothelial activation has a significant influence, not only on thrombotic complications in the immediate postoperative period (i.e. myocardial infarction, stroke and fatal pulmonary embolism), but also may regulate the long-term patient outcome [1]. In our study, we assumed that the relative risk (RR) of postoperative adverse events in the 149R allele carriers was 2.03 with a 95% confidence interval (95% CI 1.05–3.03), and that the presence of common pro-thrombotic SNPs (FV Leiden G1691A and prothrombin 20210A) did not increase the risk of adverse events ($p < 0.18$) [8].

Moreover, we observed that in 140 patients with angiographically proven two- or three-vessel CAD (mean age 65 $\pm$ $\pm$ 7.9 years), qualified to elective coronary artery bypass grafting surgery and treated with low-dose aspirin (92% of them on a dose of 75–150 mg daily), the common $\alpha$-fibrinogen p.Thr312Ala polymorphism (*FGA* c.991A>G, rs6050) influenced thrombin generation. Thrombin generation analysis was determined in platelet-poor plasma using a calibrated automated thrombogram (Thrombinoscope BV, Maastricht, The Netherlands). Each measurement comprised analysis of the

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thrombin generation and calibrator in the presence of tissue factor and phospholipids (final concentration: 5 pM and 4 $\mu$M, respectively) [9].

We observed that carriers of the Ala312 allele had a lower thrombin peak (305.6 ± 79 nM) than non-carriers (350.3 ± ± 94 nM, p = 0.002). Lag time for Ala312 carriers and non--carriers was similar (1.67 ± 0.56 min *vs* 1.60 ± 0.63 min, p = 0.4, respectively). The area under the curve did not differ between Ala312 carriers (1945 ± 1974 nM × min) *vs* non--carriers (1,827 ± 522 nM × min, p = 0.8). In the group of carriers, lower fibrinogen concentration was observed (4.0 ± ± 1.14 g/L) *vs* non-carriers (4.4 ± 1.13 g/L, p = 0.04).

In conclusion, the Ala312 polymorphism affects fibrinogen level and determines thrombin generation in patients with severe CAD on low-dose aspirin, and this effect may be related to fibrinogen concentration. Nevertheless, we cannot propose the mechanism of such a relationship. The *FGA* gene is probably located in a cluster with other genes and may affect not only fibrinogen gene expression but also other proteins in a similar manner in which *FGB* g.4884C>T (-C148T, rs1800787) influences C-reactive protein or interleukin-6 at transcriptional level [10].

There is evidence as to the role of some genetic variants and their implication in the prognosis of patients with CAD undergoing revascularisation treatment. However, we should be aware of the baseline characteristics of patients, e.g. accompanying diseases such as diabetes, hypertension or inflammatory diseases, as well as their stages. On the basis of these findings, we suggest that revealing SNPs, especially in diabetic patients, may be a useful predictor of adverse events caused by different interventional procedures.

***Conflict of interest:*** *none declared*

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