Bleeding Risk Stratification in Coronary Artery Surgery: the Should-Not-Bleed Score

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Abstract

Background

Cardiac surgery has an estimated 20% of the total blood transfusions. Of those, 11% were utilized in patients undergoing coronary artery bypass grafting (CABG) with documented wide variability in transfusion rate (7.8% to 92.8%). To address the issue of unnecessary transfusions within CABG population, we developed the model to predict the patients at low risk of bleeding who should not be transfused. Herein we present our “SHOULD-NOT-BLEED-SCORE” application developed for Windows® software platform and based on our previous research.

Methods

This study aimed to develop the user-friendly application that stratifies the patients with respect to bleeding risk. The statistical model we used in our previous research was focused on detection of CABG patients at low risk of bleeding. The rationale behind such an approach was to identify among CABG patients subgroup at low risk of bleeding. By identifying patients at low risk of bleeding we can define the subgroup of patients who should not be transfused. We developed the Windows platform application based on risk modelling we previously calculated on 1426 patients undergoing elective CABG from January 2010 to January 2018.

Results

The SHOULD-NOT-BLEED-SCORE risk score is developed for Windows software platform. The mathematical model based on multivariate analysis was used for app development. The variables that entered the scoring system were: Age; Body Mass Index; Chronic Renal Failure; Preoperative Clopidogrel Exposure; Preoperative Red Blood Cells Count; Preoperative Fibrinogen Level; Preoperative Multiplate ASPI test (AUC). The SHOULD-NOT-BLEED-SCORE identifies/predicts patients without excessive bleeding with the strong discriminatory performance (ROC analysis AUC 72.3%, p<0.001).

Conclusion

The SHOULD-NOT-BLEED risk scoring application may be useful in preoperative risk screening process. The clinical and economic burden associated with unnecessary transfusions may be adequately addressed by preoperative scoring system detecting patients at low risk of bleeding who should not be transfused.

Background

The association between severe postoperative bleeding and poor outcomes has already been widely described in literature(1-3). Transfusion of blood components in CABG patients is primarily empiric resulting inevitably in wide variability in transfusion rates between different cardiac surgery centers (range 7.8% to 92.8%)(4). This in turn results with significant economic burden and unnecessary expenditures be it from transfusion costs or costs related to transfusion associated complications, as well as overhead expenses(5, 6).

When it comes to the hemostatic management, the focus of many researchers, including our research team was to identify the patients at high risk of bleeding who might benefit from more aggressive and more targeted
haemostatic management. In patients considered to be at high risk of bleeding, the aim of hemostatic management is to provide targeted and efficient haemostatic treatment (mostly procoagulant blood components). The idea is to avoid “blind” massive transfusions and to reduce transfusion requirements with targeted, efficient transfusions.

However, high prevalence (up to 92.8%) of transfusions in patients undergoing isolated CABG, considered as lowest risk cardio-surgical procedure, raises the question to which extent those transfusions were unnecessary. The proportion of unnecessary transfusions in CABG patients climbs up to 43% resulting in overall share of 44% of overall transfusion related expenditures. Identification of patients at high risk of bleeding and shifting their hemostatic management towards more efficient and targeted transfusion treatment presents, however, only one way to reduce the unnecessary transfusions.

The other way to reduce the clinical and economic burden of unnecessary transfusions is to completely avoid transfusions in patients undergoing low risk procedures such as CABG and particularly if considered to be at low risk of bleeding at the same time. Recently, we changed our paradigm of hemostatic management and shifted our focus towards identification of low bleeding risk patients undergoing low risk procedures (ie. CABG)(5). Herein we present our institutional bleeding risk score, based on our own data and own, recently published, peer reviewed results(5). The score was embedded into “Windows” platform application with user friendly interface and was named “SHOULD-NOT-BLEED” score. The main goal of this score is to identify among patients undergoing low risk procedure such as CABG, the group of patients with estimated low risk of bleeding to whom, complete avoidance of transfusion should be considered.

In summary, the paramount idea of every hemostatic management is twofold:

1) provide targeted – efficient transfusions (avoid massive “blind” transfusions), and

2) completely avoid unnecessary transfusions.

A predictive scoring system that may stratify patients according to bleeding risk and identify target low-bleeding risk group that should not be transfused would potentially reduce the total cost of transfusion and care.

Herein, we propose our SHOULD-NOT-BLEED score calculator with aim to address the issue of negligible proportion of unnecessary transfusions in patients undergoing isolated CABG.

**Methods**

This study is designed as a proof of concept study (non-interventional) study.

We developed SHOULD-NOT-BLEED-SCORE Windows platform application. The application is grounded on the results of our recent study(5).

The SHOULD-NOT-BLEED-SCORE risk scoring tool was developed in collaboration between University of Split, University Department of Health Studies, University of Split School of Medicine, University of Zagreb - Department of Cardiac Surgery, University of Zagreb - Department of Cardiovascular Diseases, University of
Zagreb - Faculty of Economics, University of Applied Health Sciences, University of Zagreb - Division for transfusion medicine.

**Ethical Approval**

The SHOULD-NOT-BLEED-SCORE risk scoring tool is based on our previous research data that have already been published(5). The intention to develop the scoring system based on published data for which we already have approval was expressed to the Institutional Ethics committee. The Institutional Ethics committee approved the study and given the retrospective nature of the study informed written consent was waived.

**Data retrieval**

This scoring system is based on consecutive 1426 patients undergoing elective isolated CABG from January 2010 to January 2018. This database with whole blood aggregometry results is, to the best of our knowledge, the largest database of that kind worldwide.

The premise behind this scoring system is that the transfusion of different blood products in low-bleeding patients was nonessential, resulting in both unwanted consumption of blood products and unnecessary financial costs. Therefore, all blood products given to low bleeding risk patients, as well as their cost, were deemed as inappropriate and were used to determine the „saving potential”, i.e. the number and the price of blood products that can be spared if not used for unnecessary treatment of patients with low bleeding risk.

Following an extensive univariate analysis, multivariable binary logistic regression was utilized to create models predicting the low bleeding risk CABG patients. Initially created with the aim to identify patients without excessive bleeding, the developed model had specificity of as high as 94% whereas sensitivity was 24%. This is in line with the study premise necessitating the clear division of high bleeding risk patients receiving necessary blood transfusion and low bleeding risk patients where blood transfusion may, in fact, be considered unnecessary.

**Results**

In our previous and already published research(5), we performed a retrospective observational study on patients undergoing CABG with aim to define nonessential transfusions resulting in unnecessary financial costs and unwanted consumption of blood products(5). 1462 patients were included, with their demographic, laboratory, and surgical parameters being collected. Study outcomes included the extent of perioperative bleeding and the consequential transfusion rates.

Descriptive analysis of the population gave an insight into patient clinical, laboratory and surgical characteristics. As a part of the outcome analysis, the magnitude of postoperative bleeding, the transfusion rates and the financial cost of the entire patient population were also assessed. According to the magnitude of the postoperative bleeding, patients were classified into two groups: excessive-bleeding patients, defined as those exhibiting a blood loss within the upper quartile of the patient population (11.33 mL/kg or more, a value shown in our previous research(7)), and non-excessive bleeding patients, those not exhibiting the aforementioned blood loss.
As a part of our previous study and its aim, patient groups were compared according to the transfusion rates and the consequential financial costs\(^{(5)}\). Normality of distribution was assessed using Kolmogorov-Smirnov test while also plotting the distribution and accounting for skewness and kurtosis of the sample. Intergroup comparison was done using Student t test and Mann Whitney U test.

The premise of the study was that the transfusion of different blood products in non-high bleeding patients was nonessential and resulting in both unwanted consumption of a limited asset and unnecessary financial costs\(^{(5)}\). In accordance with the premise, all blood products given to the non-high bleeding patients, as well as their cost, were deemed as inappropriate. These inappropriate transfusions were used to determine the „saving potential“, i.e. the number and the price of blood products that can be spared if not used for unnecessary treatment of patients at non-high bleeding risk.

In order to determine the differences between the high and non-high bleeding patients, a group comparison was performed using Student t test, Mann Whitney U test and \(\chi^2\) test. Patients were compared across a wide variety of parameters representing their demographic, clinical, laboratory, and surgical characteristics. Patient bleeding risk in our study was defined as an affiliation with the excessive-bleeding group. Correlation analysis (using Spearman correlation coefficient) was executed to identify the potential predictors of the bleeding risk. Following an extensive univariate analysis, multivariable binary logistic regression was utilized to create models predicting the bleeding risk in a patient undergoing CABG\(^{(5)}\).

The accuracy of the generated models was evaluated using ROC analysis. Finally, based on the model accuracy, a „real-life saving potential“ (expressed both as the number and price of blood products) was derived.

Using the most accurate model and its binary logistic regression equation, a SHOULDN'T-BLEED-SCORE was generated. The score itself incorporated nine independent parameters, which were previously identified as having the strongest association with the bleeding outcome\(^{(5)}\). These parameters included five scalar (measurement) and four nominal (group) variables. Scalar parameters were as follows: patient age, patient body mass index, preoperative red blood cell count, preoperative serum fibrinogen levels and preoperative Multiplate® ASPI values. Nominal parameters were the following: existence of preoperative chronic renal failure, preoperative clopidogrel therapy and preoperative arterial hypertension associated with calcium channel blockers or ACE inhibitors use\(^{(5)}\).

The equation output stands for the probability of a patient with the given features being a high bleeder, according to the study definition. The model output was further stratified into four risk groups according to the quartile ranges of the regression equation results in our patient population. Risk groups are assigned with the following titles: low probability, intermediate probability, intermediate-high probability, high probability.

Finally, an application based on the new bleeding risk score was created for Microsoft Windows platform. In order to achieve simple input and clear result representation, Graphical User Interface was programmed in a „user friendly“ approach. Application input parameters stand for the previously mentioned, most probable patient outcome predictors. Patient age, patient body mass index (measured in kg per m\(^2\)), preoperative red blood cell count (measured exponentially as Nx10E12 per liter), preoperative fibrinogen serum levels (measured in grams per liter) and ASPI aggregation values (measured in aggregation units) have to be entered...
in exact number form. The presence of the chronic renal failure, recent clopidogrel exposure, arterial hypertension associated with calcium channel blockers or ACE inhibitors use need to be assessed, as well. The SHOULD-NOT-BLEED-SCORE result is expressed both as an absolute risk value and as risk group allocation. Color coding to sort patients according to the bleeding risk is set as follows to the risk groups are the following: low probability – green, intermediate probability – yellow, intermediate-high probability – maroon, high probability - red.

A two-tailed p value < 0.05 was considered to be statistically significant for all deployed calculations, while additional one-tailed p values were also obtained and provided for comparisons likely to result in one-directional relationships. Analysis was performed using the IBM SPSS Statistics software package (version 21). Application development was performed using Embarcadero RAD Studio software development package (XE5 version).

The URL web link to download the SHOULD-NOT-BLEED-SCORE is shown in form or QR code in Figure 2. The QR code leads user directly to the application stored on cloud and may be downloaded free of charge. The user interface is user friendly and self-explanatory so any user may easily approach and calculate the bleeding risk. SHOULD-NOT-BLEED-SCORE provides exact percentage for bleeding risk coupled with color-coding as previously described. Herein we provide two examples of calculations.

**Case scenario 1:**

An 85 years old patient presents to the emergency department with chest pain and shortness of breath. Diagnostic coronary angiography shows tight left main stenosis. Patient is on dual antiplatelet therapy (Aspirin 100 mg + clopidogrel 75 mg) given the history of vascular intervention on the right lower limb. Patient has known renal failure, BMI of 25 kg/m2, RBC count 3, Fibrinogen count of 2 and Multiplate® ASPI test of 15 AUC units (Figure 3). SHOULD-NOT-BLEED-SCORE calculates bleeding risk to be 92.14% coupled with red colored square suggesting high risk of bleeding.

**Case scenario 1 interpretation:**

This patient has a high risk for excessive bleeding. Some of the SHOULD-NOT-BLEED-SCORE parameters contributing to the risk of bleeding are invariable (*ie.* age and renal function) whereas some other parameters are modifiable (*ie.* waiting time following clopidogrel cessation, Aspirin cessation given the pronounced platelet inhibition, as assessed by Multiplate ASPI test, and management of preoperative anemia (1st pillar of the patient blood management)). The SHOULD-NOT-BLEED-SCORE is not developed to guide clinical decision-making process, but rather as a useful tool to stratify risk of bleeding and to point out parameters contributing to existing risk.

**Case scenario 2:**

A 44 years old patient is scheduled for CABG to treat triple vessels disease recently diagnosed. Patient’s BMI is 41 and has hypertension for which he takes ACE inhibitors and Calcium Channel Blockers. The lab findings show RBC 5 and Fibrinogen 4 g/L. Patient was not exposed to any antiplatelet drugs and his Multiplate® ASPI
test is 56 AUC units suggesting normal platelet function (Figure 4). SHOULD-NOT-BLEED-SCORE calculates bleeding risk to be 1.16% coupled with green colored square suggesting low risk of bleeding.

Case scenario 2 interpretation:

This patient has a low risk for excessive bleeding. All demographic and laboratory findings suggest patient should not bleed. This is an example of the patient where transfusion treatment should be avoided. Of course, this patient may experience excessive bleeding, in case of which, we should direct the bleeding management towards surgical measures (surgical cause of bleeding).

Discussion

A number of scoring methods are available for bleeding risk prediction in adult cardiac surgery(1, 8-11). However, all but WILL-BLEED risk score(1) are nonspecific addressing general adult cardiac surgery cases.

CABG represents the most common cardiac surgery procedure performed today worldwide with approximately 200,000 isolated cases per year in the US(12) and an average incidence rate of 62 per 100,000 in western European countries(13). Reported transfusion rates for isolated CABG (climbing up to over 90% with huge proportion of unnecessary transfusions) call for user-friendly screening tool to stratify bleeding risk and by identifying patients at low risk define the subgroup of patients who should not be transfused.

Few considerations are important when it comes to development of bleeding risk score:

1) Homogeneity of the study population makes it more reliable to create scoring system. We know without scoring system how complex cardiac surgery procedures carry markedly higher risk of bleeding than isolated CABG.

2) The parameters we consider when thinking of bleeding risk constantly evolve. Some of those parameters are persistent, though. However, our understanding of the bleeding risk evolves and when thinking of the inextricable association between bleeding and transfusion requirements, our focus switched from personalized point-of-care guided transfusion management in high-risk patients towards complete avoidance of transfusion in patients previously considered as to have low predicted risk of bleeding. Our bleeding risk score SHOULD-NOT-BLEED score identifies patients at low risk of bleeding with specificity of as high as 94% and sensitivity of 24%.

Having in mind how transfusion rates climb up to over 90% in CABG patients, it becomes apparent that our target was to identify CABG patients at low risk of bleeding to whom transfusion should be completely avoided.

SHOULD-NOT-BLEED score compared to other bleeding risk scores

In SHOULD-NOT-BLEED risk score calculator the ROC analysis showed an adequate discriminatory ability (AUC 0.723 95% CI (0.694-0.753), p>0.001). This discriminatory ability is comparable to WILL-BLEED score (AUC 0.725 , 95% CI 0.686-0.763, p=0.033)(1). It is important to stress out how SHOULD-NOT-BLEED score is designed to recognize patients at low risk for bleeding, whereas WILL-BLEED , as well as all other scores to
predict bleeding such as ACTION score(14), CRUSADE score(15), Papworth score(8), TRUST score(9), and TRACK bleeding score(10) were all designed to identify the patients at high risk of bleeding.

WILL BLEED bleeding risk score(1) is, to the best of our knowledge, the only score developed on the isolated CABG population. The SHOULD-NOT-BLEED score is the second one based on isolated CABG patients. Because off-pump CABG were excluded from the data analysis(5), SHOULD-NOT-BLEED score may not be applicable for patients undergoing this surgical procedure. Such an approach sounds reasonable given the fact that on-pump CABG substantially differs to off-pump CABG (the use of cardiopulmonary bypass alters haemostatic system) as well as the priority given to study cohort homogeneity.

The problem with scores being developed on the general adult cardiac surgery population is that scoring system inevitably carries non-specific parameters such as “complex cardiac surgery”. In addition to, it seems less feasible to use the same score for off-pump cases, on-pump CABG and complex aortic surgery cases. Therefore, our concept presents a kind of shift towards precise (more focused – personalized approach). Such an approach sets a priority to a homogeneity of the study cohort. The discriminatory ability of the SHOULD-NOT-BLEED score (AUC 0.723) is comparable to WILL-BLEED score (AUC 0.725)(1). In WILL-BLEED score, few baseline characteristics and information on “potent” antiplatelet drugs use allows an accurate stratification of bleeding risk(1). Our score presents more accurate assessment of preoperative haemostatic properties. We have a parameter on recent (less then 5 days) clopidogrel exposure, which is more or less the case for WILL-BLEED score. In contrast to our score, WILL-BLEED accounts for potent antiplatelet drugs exposure within 5 days. Our database of isolated elective CABG patients allowed only for assessment of recent clopidogrel exposure. This is more specific to the drug evaluated in context of bleeding risk. On the other hand, the chances to include for further studies elective patients exposed to ticagrelor are small as elective patients strictly adhere to the current guidelines on dual antiplatelet therapy. SHOULD-NOT-BLEED score provides more detailed insight into haemostatic properties. Our app is based on the single center database where all patients were exposed to Aspirin preoperatively and Aspirin was continued throughout procedure. Apparently, there was no need to put in the app whether someone was exposed to Aspirin preoperatively. However, our research group previously confirmed the presence of subset of patients who have prolonged and pronounced platelet inhibitory response to Aspirin(16), which in turn reflects bleeding tendency. We showed recently that patients with adequate platelet inhibitory response to Aspirin are prone to excessive bleeding(16). Multiplate ASPI test AUC <25 U was found to be predictive of excessive bleeding (OR 2.82 [95% CI 1.43-5.55], p=0.003) which generates the idea about the subset of patients who have pronounced platelet inhibition on Aspirin therapy and who could benefit from preoperative aspirin cessation(16). The mathematical risk modelling used as a platform for SHOULD-NOT-BLEED risk score has also proved Multiplate ASPI test value as an independent predictor of bleeding(5). SHOULD-NOT-BLEED risk score is the first bleeding risk score that accounts for drug specific platelet reactivity in calculating bleeding risk. Current guidelines on dual antiplatelet therapy suggest continuation of the Aspirin peri-procedurally (17). Our approach herein adds to the current knowledge and will hopefully contribute to change of this paradigm. It is apparent that some patients under Aspirin treatment have a higher risk of bleeding (OR 2.82), therefore, inclusion of Aspirin sensitive platelet function test into bleeding risk score calculator sets a new moment. The homogeneity of the study cohort rules out some of the confounding variables and leaves the space for some new predictors. WILL-BLEED score was designed to detect patients undergoing CABG who are at high risk of bleeding and to modify antithrombotic treatments if possible(1). In other words, the WILL-BLEED score was mainly driven by the idea that some proportion of
patients undergoing CABG are at high risk of bleeding and as such may be subject to possible haemostatic interventions, be it pre and/or intraoperative interventions. In contrast to, our SHOULD-NOT-BLEED score is driven by the idea that huge amount of transfusions (up to 93% according to the literature) in group pf patients undergoing the cardiosurgical procedure with the lowest risk such as CABG, are in fact unnecessary. The first step in addressing unnecessary transfusions in patients undergoing CABG is to identify patients primarily considered to be at low risk of bleeding. Our paradigm is that all patients with high risk of bleeding should be treated in the same/similar way using POC-guided transfusion algorithms to optimize hemostasis. The major clinical and economic burden raises from unnecessary transfusions, and when it comes to unnecessary transfusions, we should start with patients undergoing the low risk procedures such as CABG who are at the same time at low risk of bleeding.

Another advantage of SHOULD-NOT-BLEED score is it's use throughout application that is user friendly and self-explanatory. The idea of this application is not to guide and/or alter the clinical decision-making process. However, being validated and grounded on the data from primary source, this application may be useful tool for clinicians involved in preoperative screening and risk assessment.

Being based on the data from elective patients and primarily focused on elective patients makes this application not just useful tool for preoperative risk assessment, but also allows for modifiable parameters modification prior to surgery. For example, if someone is exposed to clopidogrel in close proximity to surgery and has at the same time low ASPI test value, postponing surgery with temporary discontinuation of Aspirin could modify the risk of bleeding.

The same holds for the anemic patients with low red blood cells count before surgery. The optimization of the red blood cells mass is the first pillar of the patient blood management and may easily be considered to modification if contributing to the high bleeding risk before surgery, as per SHOULD-NOT-BLEED application. On the other hand, low fibrinogen level contributing to the high risk of bleeding on calculator may advise to prompt early fibrinogen supplementation if bleeding occurs after surgery.

Furthermore, if bleeding occurs in early postoperative period (following arrival to ICU) in patient previously considered to be at low risk of bleeding, we should promptly suspect on surgical cause of bleeding and act accordingly(18). Timely decision to reexplore the patients highly suspicious to have surgical cause of bleeding makes the difference in clinical outcomes(18).

Conclusion

In conclusion, SHOULD-NOT-BLEED-SCORE bleeding risk stratification app seems to be a simple tool to stratify patients according to the bleeding risk with focus to identify CABG requiring patients at low risk for excessive bleeding. This score, as well as findings the score is based on certainly add to the current knowledge and understanding of the bleeding risk stratification. Furthermore, our app presents the step forward as may be readily available bedside, be it preadmission clinic, preadmission bay or operating theatre. We proved this concept may reduce unnecessary transfusions and avoid significant economic burden associated with unnecessary transfusions(5).
The SHOULD-NOT-BLEED bleeding risk score may serve as an impetus for further refinements in haemostatic management. Herein, we call for multicentric collaboration in further development of haemostatic management. Firstly, we propose validation of this score through multicentre collaboration. Secondly, cost-effectiveness of such score may be calculated in stepped wedge design prospective interventional multicentric trial(19).

When compared to the other three existing risk scores, the Transfusion Risk and Clinical Knowledge score had comparable or better predictive power.

When the statistical model used to design SHOULD-NOT-BLEED-SCORE was applied to our existing database, the astonishing proportion of 39.1% of transfusion costs could theoretically be reached(5). The cost savings reach 48.2% for PRBCs, 38.9% for FFP, 10.9% for platelets concentrate and 17.9% for fibrinogen, respectively(5). Aforementioned cost savings pertain solely to blood product manufacturing costs(5). Having in mind the additional cost of product administration as well as overhead expenses and the costs of treating the complications secondary to transfusion therapy itself, it becomes apparent that real-life cost savings could potentially be much higher. Notably, indirect costs of transfusion treatment may reach over 65% of all expenditures related to transfusion therapy(20, 21).

**Abbreviations**

AUC – area under the curve

BMI – body mass index

CABG – coronary artery bypass grafting

ICU – intensive care unit

US – United States

**Declarations**

*Ethics approval and consent to participate*

The study has an ethics approval (University Hospital Center Zagreb Ethics Committee Approval (8.1.-15/89-2 No 02/21/JG).

Due to retrospective non-interventional research setting, the need for written informed consent was waived.

*Availability of data and materials*

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

*Competing interests*
The authors declare that they have no competing interests in this section

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**Consent for Publication**

Not applicable

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**Authors’ contributions**

| Conceived and designed the model, analyzed and interpreted results, and drafted the manuscript and revised it critically for important intellectual content | Substantial contributions to the model design and interpretation of data | Literature overview, data acquisition, analysis and interpretation of data | Final approval of the version | Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved | Figures | Drafting the work for important intellectual content |
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| HG | | | | | | |
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Tables

**Table 1. Multivariate logistic regression model used as a mathematical platform for SHOULD-NOT-BLEED score calculator**

|                        | Exp(B) | 95% C.I.for EXP(B) | Sig.     |
|------------------------|--------|--------------------|----------|
|                        |        | Lower              | Upper    |
| Age (Years)            | 0,972  | 0,957              | 0,988    | 0,001    |
| Body Mass Index        | 1,170  | 1,129              | 1,213    | <0,001   |
| Chronic Renal Failure  | 0,541  | 0,299              | 0,979    | 0,042    |
| Clopidogrel Exposure   | 0,627  | 0,463              | 0,850    | 0,003    |
| Calcium Channel Blockers | 1,371 | 1,050              | 1,788    | 0,020    |
| ACE inhibitors         | 1,393  | 1,053              | 1,842    | 0,020    |
| Red Blood Cells Count  | 1,319  | 1,015              | 1,715    | 0,039    |
| Fibrinogen             | 1,321  | 1,162              | 1,503    | <0,001   |
| ASPI Multiplate        | 1,010  | 1,005              | 1,016    | <0,001   |
| agregometry test (AUC) |        |                    |          |          |
| Constant               | 0,012  |                    | <0,001   |