# Predictive Factors Driving Positive Awake Test in Carotid Endarterectomy Using Machine Learning

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Running title: Machine Learning Predictor of Positive Awake Test

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**ABSTRACT**

OBJECTIVES

Positive neurologic awake testing during the carotid cross-clamping may be present in around 8% of patients undergoing carotid endarterectomy (CEA). The present work aimed to assess the accuracy of an artificial intelligence (AI)-powered risk calculator in predicting intraoperative neurologic deficits (IND).

METHODS

Data was collected from carotid interventions performed between January 2012 and January 2023 under regional anesthesia. Patients with IND were selected along with consecutive controls without IND in a case-control study design. A predictive model for IND was developed using machine learning (ML), specifically Extreme Gradient Boosting (XGBoost) model, and its performance was assessed and compared to an existing predictive model. Shapley Additive exPlanations (SHAP) analysis was employed for the model interpretation.

RESULTS

Among 216 patients, 108 experienced IND during CEA. The AI-based predictive model achieved a robust area under the curve (AUC) of 0.82, with an accuracy of 0.75, precision of 0.88, sensitivity of 0.59, and F1Score of 0.71. High body mass index (BMI) increased contralateral carotid stenosis, and a history of limb paresis or plegia were significant IND risk factors. Elevated preoperative platelet and haemoglobin levels were associated with reduced IND risk.

CONCLUSIONS

This AI model provides precise IND prediction in CEA, enabling tailored interventions for high-risk patients and ultimately improving surgical outcomes. BMI, contralateral stenosis, and selected blood parameters emerged as pivotal predictors, bringing significant advancements to

decision-making in CEA procedures. Further validation in larger cohorts is essential for broader clinical implementation.

Keywords: [Carotid stenosis; intraoperative neurologic deficits; perioperative stroke; regional anesthesia].

**ABREVIATION LIST**

| | |
|---|---|
| AI | Artificial intelligence |
| AUC | Area Under the curve |
| BMI | Body mass index |
| CACC | Carotid cross-clamping |
| CCA | Common carotid artery |
| CEA | Carotid endarterectomy |
| CKD | Chronic kidney disease |
| GA | General anesthesia |
| IND | Intraoperative Neurologic deficits |
| IQR | Interquartile range |
| MI | Myocardial infarction |
| ML | Machine Learning |
| RA | Regional anesthesia |
| SD | Standard deviation |
| SHAP | Shapley Additive exPlanations |
| XGBoost | Extreme Gradient Boosting (algorithm) |

## 1. INTRODUCTION

Carotid endarterectomy (CEA) is a well-established and cost-effective treatment for asymptomatic or symptomatic carotid artery stenosis. Despite advancements in endovascular technique, it remains the preferred treatment option [1]. This technique is primarily done for the prevention of stroke in these patients and further being capable of reducing healthcare costs. The risk of perioperative complications, such as stroke, myocardial infarction (MI), or death, ranges from 2% to 6% [2].

During CEA, carotid artery cross-clamping (CACC) might potentially cause intraoperative neurologic deficits (IND) [3]. For every 10 minutes of increased time during arterial clamping, a higher risk of 30-day cerebrovascular and mortality events has been described, irrespective of shunt use [4]. Most intraoperative ischemic changes can be attributed to embolization, with approximately 10% associated with hemodynamic factors [5, 6]. In the event of any observed IND, timely implementation of shunting is recommended by some authors [7]. The described predictive factors in literature for IND include a body max index (BMI) superior to 30 $Kg/m^2$, a higher contralateral carotid stenosis degree, and a lower degree of ipsilateral stenosis [3, 8].

There is a lack of statistically significant differences in stroke, MI, and mortality rates between CEA performed under general (GA) or regional anesthesia (RA) [3, 9]. However, a major advantage of RA is that it allows continuous neurological monitoring with the awake test, which is considered the gold standard for assessing neurologic function during CACC in patients undergoing CEA [3, 10]. Several cerebral monitoring techniques, mainly described under GA, are available, such as transcranial Doppler ultrasound, electroencephalogram, stump pressure, and somatosensorial evoked potentials [6, 11, 12]. In the last network meta-analysis including almost 17 studies and 21 538 patients, although the current evidence lacks high-quality data, none of the results have shown significant differences between all monitoring tools and the awake test  regarding stroke and mortality, [12]. Additionally, these methods exhibit low sensitivity for detecting insufficient brain blood flow and intraoperative stroke [6, 11]. It has been described that the near-infrared spectroscopy test used alone compared to the awake test may not be sensitive or specific enough to predict postoperative strokes [5].

A positive awake test is a classic indicator for shunt placement, which increases the risk of major adverse events like stroke and postoperative complications [8, 10]. Other indirectly studied risk factors for the shunting option include elderly patients above 75 years of age, symptomatic disease, and the female sex [13]. Therefore, perioperative stroke emerges as the most concerning complication following CEA, emphasizing the need for effective preventive measures during the surgery [10, 14].

Artificial intelligence (AI) has demonstrated the potential as a valuable predictor of outcomes in CEA [15]. Utilizing machine learning (ML) algorithms, AI enables accurate prediction of ischemic events [15], identification of high-risk patients [16], and assessment of mortality risk [17]. These advancements in AI-based prediction models offer opportunities for improved clinical assessment and personalized treatment in CEA procedures.

This study investigates the effectiveness and feasibility of AI techniques to predict positive awake tests in CEA to enhance surgical decision-making and patient outcomes.

## 2. METHODS

This study was approved by the University's Institutional Review Board (248-18), which respects the Declaration of Helsinki, and the Ethics Committee waived informed consent. The cohort was registered for patient enrolment at clinicaltrials.gov (NCT04347785).

### *2.1 Study Population*

Patients who underwent CEA under regional anesthesia at a tertiary referral center between January 2012 and January 2023, and who had a positive awake test, were consecutively included in the study. Patients in the control group were selected with a 1:1 ratio as the immediately consecutive patient submitted to CEA without the above-mentioned primary outcome in a case-control study design. The presence of synchronous cardiac surgery or the patient's *a priori* unwillingness to stay awake during the intervention were reasons for exclusion from the study (Figure 1). Patients with any contraindication for RA were also excluded (<1% of all patients, mostly perceived patient unwillingness). Data collection, such as demographics and comorbidities, were assessed through clinical registries. This study was reported according to the Developmental and Exploratory Clinical Investigations of DEcision support systems driven by Artificial Intelligence (DECIDE-AI) guideline [18].

### *2.2 Preoperative assessment*

Two consecutive duplex ultrasound exams or a computed tomography angiogram were performed for carotid stenosis diagnosis.

Patients were evaluated before surgery by a vascular surgeon and an anesthesiologist. When previously symptomatic, a neurology appointment was performed. Heart rate and tensional values were measured during patient's admission to the hospital. All the patients were under statins, single antiplatelet (189 patients), or dual antiplatelet therapy (twenty-seven patients) before surgery.

*2.3 Postoperative management*

All patients were evaluated resorting to clinical examination and Doppler ultrasound at 30 to 90 days after discharge and 12 months of follow-up.

*2.4 Definitions*

The awake test, conducted by the anesthesiologist every three minutes during surgery, involved verbal prompts for speech (e.g. name, address), requests for limb movement, and leg tactile stimulation to assess sensory perception. A positive "awake test" (IND) was defined as any “de novo” persistent symptomatic change or sign at neurologic examination (speech, motor function, and consciousness) during CACC, after anesthesiologic therapeutic review and pharmacologic hemodynamic readjustment [19]. The anesthesia and surgery team settled the event diagnosis jointly.

Carotid stenosis was considered symptomatic or asymptomatic according to the clinical practice guidelines of the European Society of Vascular Surgery [20]. Diagnosis criteria of carotid stenosis was followed by resorting to duplex ultrasound, computed tomographic angiography and/or magnetic resonance angiography to identify and characterize the extent of the disease [20]. Chronic kidney disease (CKD) was defined as an established diagnosis of CKD or a basal creatinine ≥ 1.5mg/dl.

*2.5 Surgical technique and anesthesia approach*

The surgical technique consisted of CEA followed by patch angioplasty, eversion technique, or direct suture. The technique used depended on the choice of the operating surgeon.

Intraoperative neurologic monitoring consisted of consecutive brief awake neurological examinations and surveillance every 3 minutes during CACC. The neurological examinations prevailed in the definition of IND events [21].

## 3. THEORY AND CALCULATION

### *3.1 Statistical Analysis*

#### 3.1.1 Bivariable analysis

The necessary sample for an Area Under the Curve (AUC) assessment was calculated resorting to online Sample Size Calculators for Designing Clinical Research (https://sample-size.net/ - aiming for AUC >80%. A total sample of 100 patients was reached. Current recommendations endorse using a minimum of 100 events and 100 non-events as it allows enough power (80%) to detect whether the predictive accuracy is different from a pre-specified null hypothesis value [22].

The bivariate analysis was performed with SPSS (IBM Corp., released 2021. IBM SPSS Statistics for Windows, version 28.0, Armonk, NY, USA). The distribution of continuous variables was assessed through skewness and kurtosis distribution tools. For a normal continuous variable distribution, mean ± standard deviation (SD) and median [interquartile range (IQR) percentile 25 - percentile 75] were assessed for description. Note that for asymmetric distributions, median [IQR] calculation was preferred. Categorical variables were displayed as n (%) in function of the dependent variable. Inferential comparisons in the bivariable analysis were performed using the chi-square test (or Fisher's tests, if conditions were violated) for both categorical variables, and Student's t test or Mann-Whitney U test, depending on normality when a variable is continuous. A P-value inferior to 0.05 was considered statistically significant.

### *3.2 Data understanding and preparation*

This work followed the cross-industry standard process model for data-mining [23] using Python and standard packages employed in Data Science like NumPy [24], Pandas [25], Matplotlib [26], and Seaborn [27]. Following this process model, prior to modeling, it was necessary to understand the predictive domain and the data fully. The exploratory data analysis determined that the overall quality of the data was good, with missing values in each variable below 1%. The only substantial issue was the existence of missing values in some variables, like cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), or triglycerides. The columns with more than 5% of missing values were removed from the dataset to overcome this issue. Since feature selection, particularly feature engineering contributes positively to the accuracy of prediction models [28, 29], several analyses were made to select variables, including Pearson's correlation, distribution measurement, and importance analysis in assessing several models. These operations resulted in the creation of a new variable, named ratio of the neutrophiles by the lymphocytes (ratioNeu_Lym), and the removal of several variables.

### 3.2.1 Modeling

ML, enables computers to learn from data, identify complex patterns, and make predictions without explicit programming. The choice of ML over other modeling options is justified by its ability to capture complex relationships among data and maintain high predictive accuracy [30].

One of the main challenges of this study was to build a ML model with a small dataset (n=216). To overcome this challenge, a cross-validation approach was employed. Cross-validation is a widely used technique for evaluating the performance of ML models, particularly when the available dataset is small. In cross-validation, the available data is divided into multiple subsets or folds. The model is then trained on all but one of these folds, and the remaining fold is used as a validation set to evaluate the model's performance. This process is repeated multiple times, with each fold serving as the validation set once. The results from each iteration are then averaged to produce an overall performance estimate for the model [31].

The applied modeling process involved the application of the Optuna package [32] and the Python implementation of the Extreme Gradient Boosting (XGboost) algorithm [33] in a 10-fold cross-validation of 10,000 iterations to hyper-tune the parameters to use on the fine model. XGBoost is a scalable, distributed gradient-boosted decision tree ML library [33]. This model provides parallel tree boosting and is the leading ML library for regression, classification, and ranking problems [29]. The optimal hyperparameters were identified through a “random search” approach. The score was then calculated by obtaining the best coefficient of variation, i.e., by dividing the SD of the 10-folds over the respective mean. The final XGBoost model was trained using the entire dataset, using the best 10-fold cross-validation iteration parameters (Supplemental Table 1).

To identify the drivers that allow the prediction IND, the authors employed the SHAP (Shapley Additive exPlanations) [34] model on top of the predictive model. SHAP is a game-theoretic approach to explain the output of a predictive model by measuring each feature's contribution to the model's predictions. The variables importance in predicting IND is shown by descending order, from top to bottom. A mean SHAP value representing each variable's magnitude of contribution to the occurrence of IND was displayed in a chart, where blue data points indicate that the instance has low values, while red data points indicate that the instance has high values. In addition, a heatmap representing a hierarchical clustering of data, where a color represents each patient SHAP value by feature, was also performed. The rows (patients) and columns (features) are rearranged to display similar values near each other according to the hierarchical clustering. The cluster map was created using the Seaborn package [27] and the Euclidean distance as the measure of distance.

## 4. RESULTS

*4.1 Demographic and clinical data*

The study population (n=216) mainly was male (73.3% vs. 19.8%), with an overall mean age of 70.5 ± 8.9 years. Both groups included 108 patients, and comparison between the groups are displayed in Table 1.

Cardiovascular risk factors (Table 1) for both groups were comparable, except for obesity and triglyceride levels. Patients who experienced IND were significantly more obese than controls (30.3% vs. 9.3%, P=0.001) but had a lower mean triglyceride level (P=0.023). The mean number of antihypertensive drugs taken and patients taking beta blockers or aspirin over two weeks were also comparable between groups. Both groups were similar regarding the preoperative hematologic parameters (Table 2).

Patients with IND presented a lower degree of ipsilateral carotid stenosis (81.9% vs. 85.5%, P=0.012) but an increased contralateral stenosis degree of 66.7% (vs. 59.1%, P=0.001), as shown in Table 1. IND patients had a higher prevalence of symptomatic disease (47.2% vs. 43.0%), although this difference was not statistically significant (P=0.789).

*4.2 Predictive model*

The predictive model achieved an AUC of 0.82 (Figure 2), with the best Youden's index calculated at 0.5093, which was achieved at a threshold of 0.54. As presented in Supplemental Table 2, the number of False Positives (Type I error) was very low (n=9), expressing increased specificity. However, the number of False Negatives (Type II error) was relatively high (n=44). Even so, the model has reached good results, attaining 0.75 in Accuracy, 0.88 in Precision, 0.59 in Sensitivity, which resulted in an F1Score of 0.71.

The programming code of the created model can be assessed through the link https://osf.io/dx9up/?view_only=11bc2e5078c048f18036a6c37566987d.

*4.3 Model's interpretation*

Figure 3 shows the SHAP summary plot. In the figure, each data point represents an instance. The mean SHAP value by a variable is further detailed in Figure 4. High negative SHAP values (on the x-axis) indicate a contribution to a lower presence of IND, while high positive SHAP values indicate a contribution to a higher presence of IND. Having this in consideration, higher values are seen in obesity, contralateral carotid stenosis, and preoperative limb paresis, tending to carry a higher probability of resulting in IND. On the contrary, higher values of preoperative platelet count, haemoglobin, and ipsilateral carotid stenosis tend to have a high probability of not resulting in IND. In fact, only 10 of the 16 employed variables have some predictive power.

Figure 5 presents the cluster map. Besides the obvious clusters by patients based on their outcome, it is possible to verify the creation of several sub-clusters.

If IND is not present, it is possible to observe two main sub-clusters. One of those clusters presents just three observations with patients with non-obese patients but with high values of contralateral stenosis. The other sub-cluster divides again into two other sub-clusters. One of those is composed of obese patients. If IND is present, one sub-cluster of higher contralateral stenosis is identified within patients with IND, regardless of the BMI level. Additionally, another cluster of patients with IND is defined by obesity.

## 5. DISCUSSION

*5.1 Main findings summary and AI modeling*

Using ML, it was possible to obtain a precise IND prediction in CEA achieving an AUC of 0.82. Concerning the XGBoost model, studies have demonstrated that it is a versatile ML algorithm, which excels in predicting outcomes following CEA, by simplifying complex clinical decisions [35]. It consistently outperforms alternatives like logistic regression, offering enhanced predictive accuracy with an AUC of 0.90 for 1-year stroke or death in CEA [35].

In this study, three clinical variables were associated with higher rates of IND in patients submitted to CEA under RA – obesity, higher degrees of contralateral carotid stenosis and prior contralateral limb paresis or plegia, being the former two of highest importance of contribution. On the other hand, increased levels of preoperative haemoglobin, platelets, and a higher degree of ipsilateral stenosis demonstrated to play a protective role.

*5.2 Predictive factors*

Obesity was the variable that contributed the most to the outcome and similar findings were previously described [3, 8, 36]. Not only is it associated with a higher prevalence of other comorbidities, but it also predisposes patients to surgical complications [37, 38] and might increase technical complexity since more adipose tissue implies more surgical manipulation and additional tissue dissection. In a large cohort study with >25000 patients submitted to CEA, metabolic syndrome was found to increase the odds of developing cardiocerebrovascular events [39]. Increased BMI has also been associated as an independent risk factor for higher degrees of tortuosity of carotid arteries, which may trigger cerebral ischemia during vascular procedures [40].

Another significant result of this work was the strong contribution of the higher degrees of contralateral carotid stenosis for IND incidence, in concordance with previous studies of the authors [3, 8, 36, 41]. The GALA trial advocates a similar trend between contralateral disease and cerebrovascular events, whereas perioperative stroke is extensively described in the literature [42].

In a lesser extent of magnitude, the presence of preoperative limb paresis, implying previous cerebrovascular events, is associated with a higher risk of IND [43]. This could be explained by established hemodynamic impairment due to affected middle cerebral artery velocity, with critically hypoperfused territories and compromised collateral pathways [44, 45].

### *5.3 Protective factors*

Conversely, patients presenting a higher degree of ipsilateral carotid stenosis seem to be related to a decreased risk of IND. As previously observed in other observational studies [3, 36], this finding could be explained by the overtime development of vascular collateral pathways. Nonetheless, 80% of these patients are in a chronic state of cerebral hypoperfusion, reflecting a more resilient state when CACC is applied, especially for degrees above 90% [46, 47].

Higher haemoglobin and platelet levels were shown to display a protective role in the incidence of IND. It is known that adequate platelet level accelerates innate regenerative processes, contributing to neuronal protection [48, 49]. Pothof et al. [50] conducted a large observational study of 16068 patients submitted to CEA under GA and described a 3-fold increased risk of 30-day mortality in symptomatic patients with preoperative anemia impairing oxygenation of cells occurs during CACC. A trend to higher application of shunting was verified in anemic patients, regardless of symptomatic status. Hence, prior optimization with iron supplements or erythropoietin prescription  might be beneficial [51].

### *5.4 Treatment strategies*

Knowing a patient's heightened risk could prompt more rigorous evaluation and discussion of alternative strategies, as the risk of stroke could reach prohibitive levels—up to 14%, questioning the potential benefits of CEA [8]. Some factors, such as haemoglobin, platelets and myocardial function, could be optimized before the intervention. A recent trial has demonstrated that targeted nutritional support might be beneficial in these patients to improve clinical and biochemical parameters to achieve better outcomes [52]. Considerations about other viable techniques without blood flow interruption and acceptable results, such as transcarotid or transfemoral revascularizations could be made [8, 53, 54].

### *5.5 Limitations of the study*

While the present study has offered valuable insights, it is essential to acknowledge its limitations. Firstly, sample size is from a single tertiary referral center, limiting the generalization of the findings, as patients here tend to have more complex medical histories. Secondly, another important potential limitation of this study is the selection of controls in 1:1 ratio for this rare event of positive IND, which might introduce selection bias and could potentially overestimate the perceived risk of symptoms and skew the study outcomes. Additionally, differences among surgical teams such as experience and techniques were also not assessed. Another key limitation is the absence of external validation, which is crucial given the dominance of the positive class in our dataset. This limitation could impact the statistical robustness and external validity with a risk of overfitting the model.

## 6. CONCLUSION

The XGBoost model achieved an AUC of 0.82, identifying key predictors of IND during CEA under RA, including higher BMI, contralateral carotid stenosis, limb paresis/plegia, and protective features, such as higher preoperative platelets and haemoglobin levels and a greater degree of ipsilateral carotid stenosis. The AI tools show promise in assisting surgeons in tailoring the best approach by identifying at-risk patients' profiles. However, further validation in larger samples is needed.

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## 8. FIGURE LEGENDS

**Figure 1.** Flow-diagram of the study design.

CEA – Carotid Endarterectomy; CS – Carotid Stenosis; IND – Intraoperative neurologic deficits; RA – Regional Anesthesia;

**Figure 2.** ROC of Xgboost for intraoperative neurologic deficits during carotid endarterectomy.

**Figure 3.** SHAP summary plot.

PreOp erythrocytes - preoperative erythrocytes; PreOp heart rate – preoperative heart rate; PreOp paresis – preoperative paresis; PreOp platelet count – preoperative platelet count; ratioNeu_Lym - neutrophil/lymphocyte ratio; RDW-CV – red blood cell distribution width-coefficient of variation.

**Figure 4**. Mean SHAP value.

PreOp erythrocytes - preoperative erythrocytes; PreOp heart rate – preoperative heart rate; PreOp paresis – preoperative paresis; PreOp platelet count – preoperative platelet count; ratioNeu_Lym - neutrophil/lymphocyte ratio; RDW-CV - red blood cell distribution width-coefficient of variation.

**Figure 5.** Cluster map of all observations by feature's SHAP importance.

IND – intraoperative neurologic deficits; PreOp erythrocytes - preoperative erythrocytes; PreOp heart rate – preoperative heart rate; PreOp paresis – preoperative paresis; PreOp platelet count – preoperative platelet count; ratioNeu_Lym - neutrophil/lymphocyte ratio; RDW-CV - red blood cell distribution width-coefficient of variation.

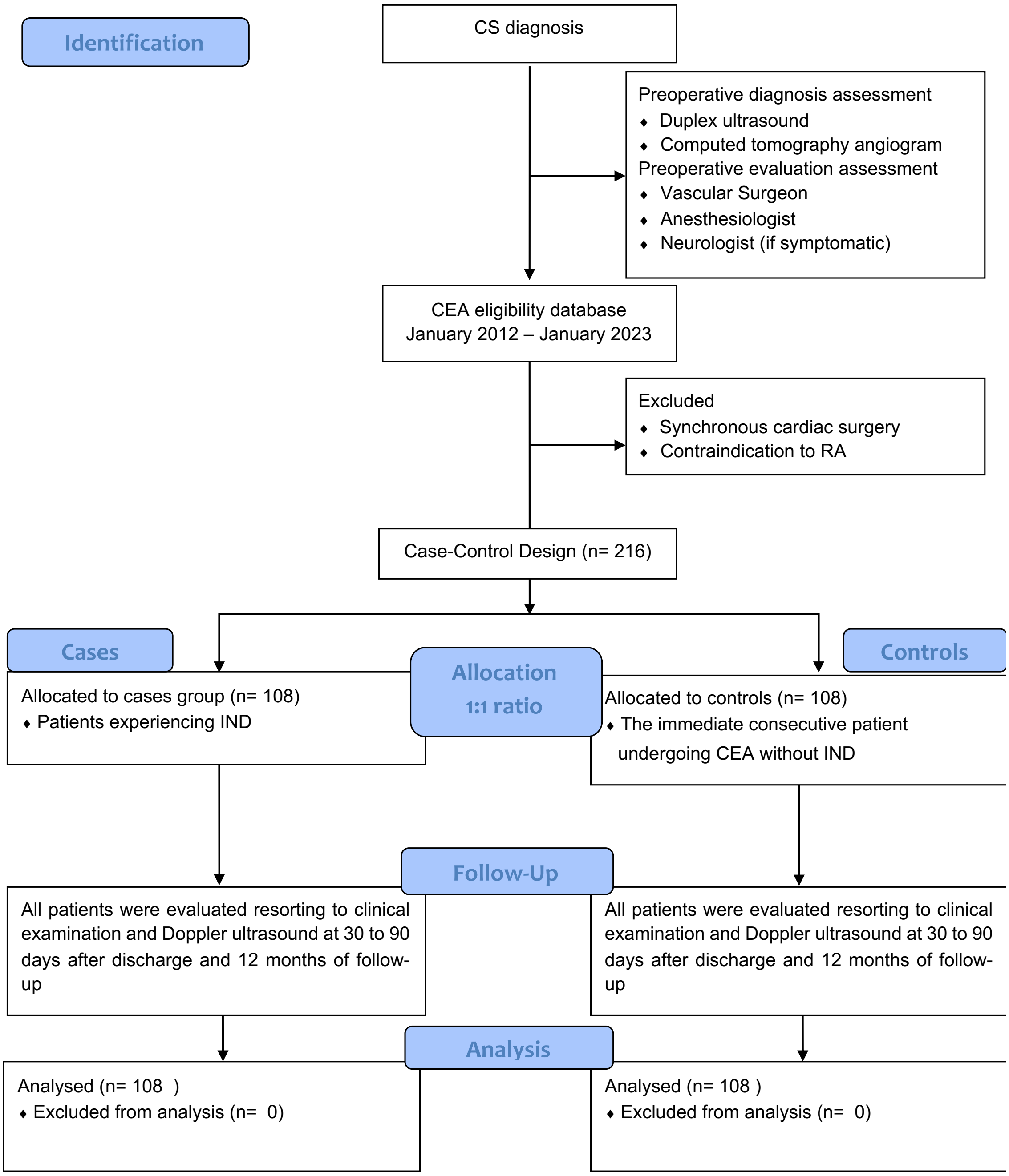



Figure 1 – Flow diagram of the designed study.

**Table 1.** Demographics, comorbidities and binary analysis

| | **Total** (n=216) | **Control** (n=108) | **IND** (n=108) | ***p-value*** |
|---|---|---|---|---|
| **Gender, n (%)** | | | | |
| Male | 170 (73.3) | 90 (84.1) | 80 (73.4) | 0.054$^*$ |
| Female | 46 (19.8) | 17 (15.9) | 29 (26.6) | |
| **Age (years)** | | | | |
| Mean (±SD)$^*$ | 70.5 (±8.9) | 69.3 (±8.60) | 71.6 (±9.14) | 0.054 |
| Median (IQR)$^?$ | 72.0 (14.0) | 71.0 (14.0) | 72.0 (13.0) | |
| **HR, Mean (±SD)**$^*$ | 67.0 (±14.1) | 65.6 (±11.9) | 68.4 (±15.8) | 0.150 |
| **Side** | | | | |
| Right, n (%) | 104 (48.1) | 58 (54.2) | 46 (42.2) | 0.078$^*$ |
| Left, n (%) | 112 (51.9) | 49 (45.8) | 63 (57.8) | |
| **CV risk-factors** | | | | |
| Hypertension, n (%) | 191 (88.4) | 94 (87.9) | 97 (89.0) | 0.793$^*$ |
| Diabetes, n (%) | 90 (41.7) | 42 (39.3) | 48(44.0) | 0.476$^*$ |
| Smoking history, n (%) | 112 (51.9) | 61 (57.0) | 51 (46.8) | 0.133$^*$ |
| Dyslipidemia, n (%) | 188 (87.0) | 92 (86.0) | 96 (88.1) | 0.647$^*$ |
| Cholesterol, Mean (±SD) | 181.3 (±48.6) | 182.2 (±49.4) | 180.5 (±48.1) | 0.706 |
| HDL, Mean (±SD) | 43.6 (±13.5) | 44.4 (±14.1) | 42.9 (±12.8) | 0.522 |
| LDL, Mean (±SD) | 115.2 (±79.2) | 119.3 (±104.1) | 111.0 (±39.2) | 0.254 |
| Triglycerides, Mean (±SD) | 142.7 (±66.2) | 143.8 (±75.0) | 141.7 (±56.2) | 0.023 |
| Obesity, n (%) | 43 (19.9) | 10 (9.3) | 33 (30.3) | 0.001$^*$ |
| CKD, n (%) | 26 (12.0) | 13 (12.1) | 13 (11.9) | 0.960$^*$ |
| Creatinine, Mean (±SD) | 0.99 (±0.58) | 1.01 (±0.72) | 0.967 (±0.40) | 0.583 |
| PAD, n (%) | 54 (25.0) | 29 (27.1) | 25 (22.9) | 0.479$^*$ |
| CAD, n (%) | 76 (32.1) | 37 (34.6) | 39 (35.8) | 0.853$^*$ |
| COPD, n (%) | 30 (13.9) | 18 (16.8) | 12 (11.0) | 1.394$^*$ |
| EF <40, n (%) | 27 (12.5) | 12 (11.2) | 15 (13.8) | 0.572$^*$ |
| AF, n (%) | 15 (7.0) | 7 (6.5) | 8 (7.4) | 0.803$^*$ |
| **ASA, n (%)** | | | | |
| II | 35 (17.5) | 19 (19.0) | 16 (16.0) | 0.742$^*$ |
| III | 153 (76.5) | 76 (76.0) | 77 (77.0) | |
| IV | 12 (6.0) | 5 (5.0) | 7 (7.0) | |
| **Functional status, n (%)** | | | | |
| Dependent | 6 (2.8) | 2 (1.9) | 4 (3.7) | 0.238$^*$ |
| Partially dependent | 25 (11.6) | 9 (8.4) | 16 (14.7) | |
| Independent | 185 (85.6) | 96 (89.7) | 89 (41.7) | |
| Asymptomatic, n (%) | 118 (54.9) | 61 (57.0) | 57 (52.8) | |
| Symptomatic, n (%) | | | | |
| TIA | 24 (11.2) | 12 (11.2) | 12 (11.1) | 0.789$^*$ |
| Stroke | 73 (34.0) | 34 (31.8) | 39 (36.1) | |
| **Preoperative limb** | | | | |
| Plegia | 55 (25.5) | 20 (18.7) | 35 (32.7) | 0.06$^*$ |
| Paresis | 7 (3.2) | 1 (0.9) | 6 (5.6) | |
| **Stenosis degree** | 83.7±10.3 | 85.5±9.6 | 81.9±10.7 | |
| Mean (±SD) (%) | | | | 0.012 |
| **Contralateral stenosis degree** | | | | |

| | | | | |
|---|---|---|---|---|
| Mean (±SD) (%) | 62.9±18.6 | 59.1±14.7 | 66.7±21.1 | 0.001 |
| **Contralateral stenosis** | | | | |
| (>50%) | 103 (50.7) | 44 (43.6) | 59 (57.8) | 0.042* |
| (>70%) | 39 (19.2) | 13 (12.9) | 26 (25.5) | 0.023* |
| **Anti-Hipertensive agents** | | | | |
| Number, Mean (±SD) | 2.02 (±1.24) | 2.05(±1.2) | 1.99 (1.26) | 0.731 |
| Beta Blocker, n (%) | 62 (31.3) | 36 (36.7) | 26 (26.0) | 0.103* |
| **AAS >2 weeks,** n (%) | 139 (65.3) | 64 (61) | 75 (69.4) | 0.193 |

* - Pearson's chi-squared test

Abbreviations: AAS - Acetylsalicylic acid for more than two weeks before surgery; AF - atrial fibrillation; ASA - American Society of Anesthesiologists Physical Status Classification System; BMI - body mass index; CAD - coronary artery disease; CHF - cardiac heart failure; CKD - chronic kidney disease (creatinine 1.5 mg/dL); COPD - chronic obstructive pulmonary disease; CV - cardiovascular; EF - ejection fraction; HDL - high-density lipoprotein; HR - heart rate; IND - alterations on the neurologic examination during carotid clamping; IQR - interquartile range (25–75%); LDL - low-density lipoprotein; obesity - body mass index > 30 kg/m$^2$; PAD - peripheral artery disease; SD - standard deviation; TIA - transient ischemic attack.

**Table 2.** Preoperative hematologic parameters

| | **Total** (n=216) | **Control** (n=108) | **IND** (n=108) | ***p-value*** |
|---|---|---|---|---|
| Hemoglobin (g/dL) | 13.2 (±1.9) | 13.2 (±2.0) | 13.2 (±1.8) | 0.314* |
| MCHC (g/dL) | 33.7 (±1.2) | 33.9 (±1.1) | 33.6 (±1.2) | 0.504* |
| RDW-CV (%) | 13.57 (±1.3) | 13.3 (1.2) | 13.3 (1.7) | 0.065* |
| RDW-SD (fL) | 44.3 (±4.5) | 43.5 (4.9) | 43.8 (4.1) | 0.870* |
| Lymphocyte count | 2.0 (±0.7) | 2.1 (±0.7) | 1.9 (±0.7) | 0.797* |
| Lymphocyte (%) | 27.7 (±8.8) | 28.7 (±9.0) | 26.7 (±8.5) | 0.545* |
| Neutrophil count | 4.5 (2.1) | 4.3 (1.8) | 4.5 (2.2) | 0.423¤ |
| Neutrophil (%) | 60.6 (±9.9) | 59.5 (±10.0) | 61.7 (±9.8) | 0.666* |
| Platelet count | 211.0 (83.0) | 206.5 (86.0) | 213.0 (82.5) | 0.819¤ |
| MPV (fL) | 11.0 (±0.9) | 10.9 (±0.96) | 11.0 (±0.91) | 0.145* |
| PDW (fL) | 13.3 (±2.3) | 12.9 (2.73) | 13.0 (2.8) | 0.615¤ |
| Neutrophil/lymphocyte ratio | 2.3 (1.6) | 2.1 (1.6) | 2.3 (1.5) | 0.109¤ |
| Platelet/lymphocyte ratio | 113.4 (69.3) | 101.1 (71.9) | 114.2 (65.5) | 0.084¤ |
| Haemoglobin/platelet ratio | 0.1 (±0.0) | 0.1 (±0.0) | 0.1 (±0.0) | 0.489 |
| PDW / platelet ratio (fL) | 0.06 (0.0) | 0.1 (0.0) | 0.1 (0.0) | 0.778¤ |
| RDW-CV / platelet ratio (%) | 13.3 (3.1) | 6.3 (2.3) | 6.3 (3.2) | 0.769¤ |

* – T-test; ¤ - Mann–Whitney U test;
IND – neurologic deficits; MCHC - mean corpuscular hemoglobin concentration; MPV - mean platelet volume; PDW - platelet distribution width; RDW-CV - red blood cell distribution width-coefficient of variation; RDW-SD - red blood cell distribution width - standard deviation.

Figure 2

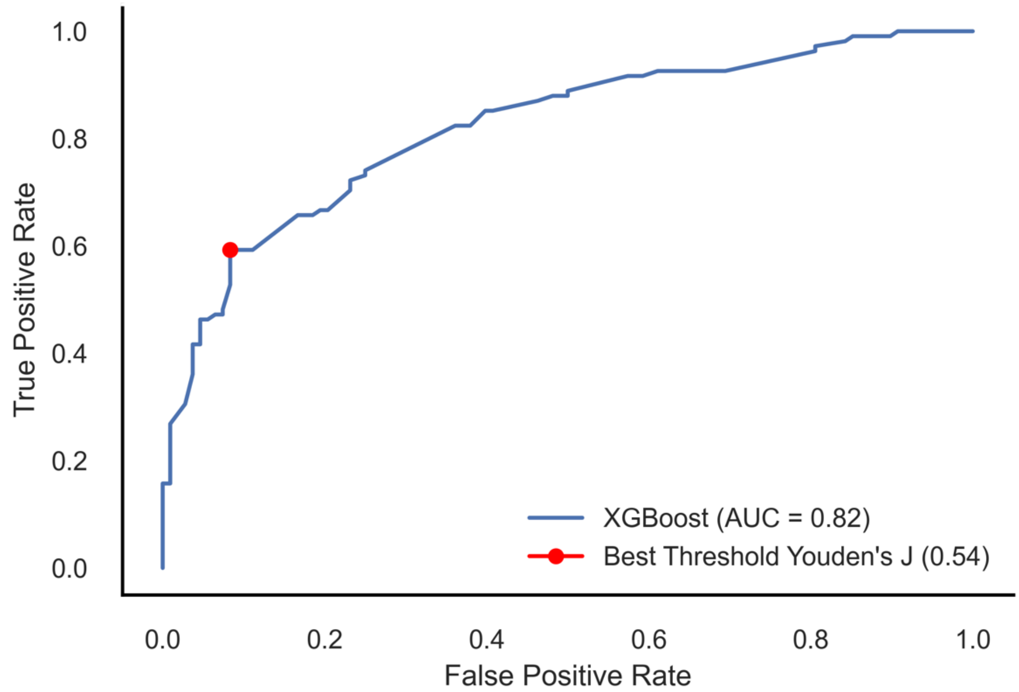

1.0
0.8
0.6
0.4
0.2
0.0
True Positive Rate
0.0
0.2
0.4
0.6
0.8
1.0
False Positive Rate
XGBoost (AUC = 0.82)
Best Threshold Youden's J (0.54)

Figure 3

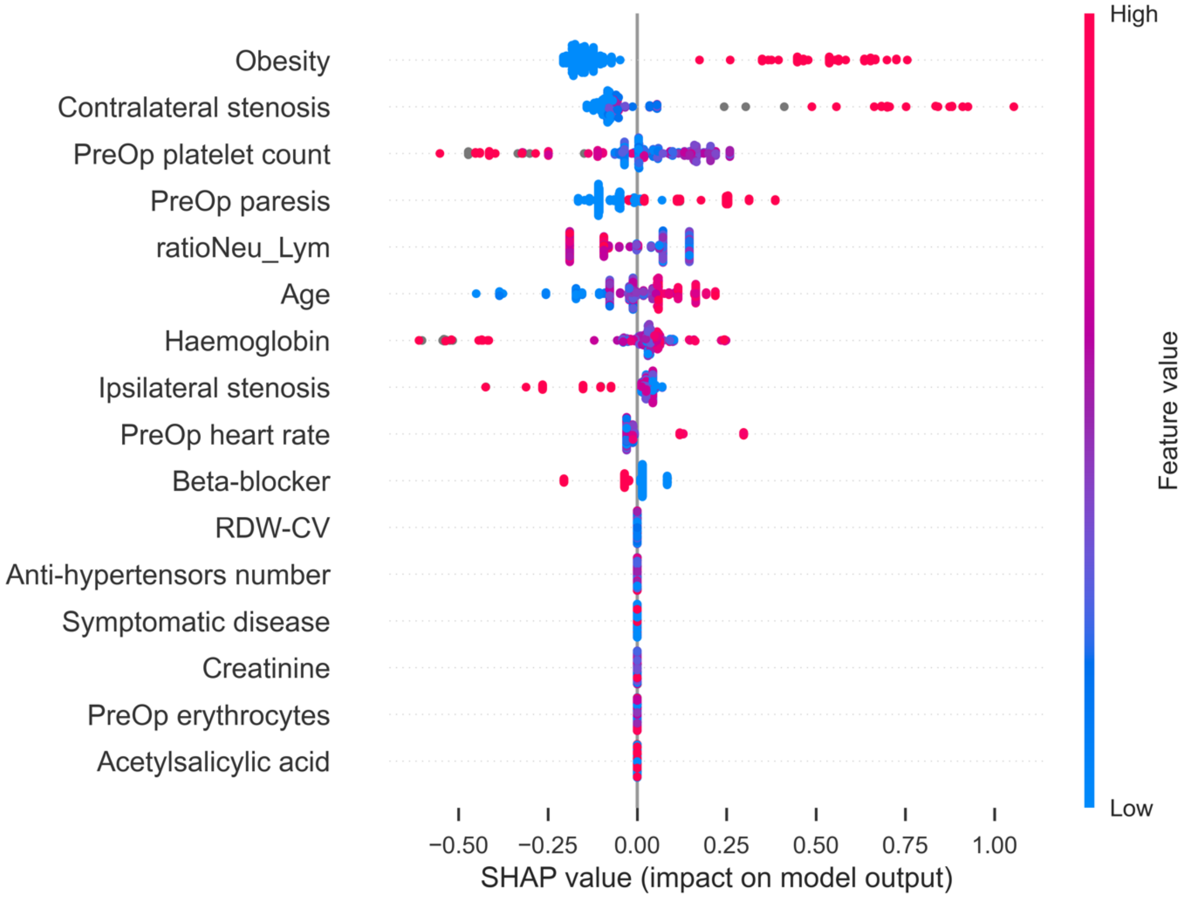
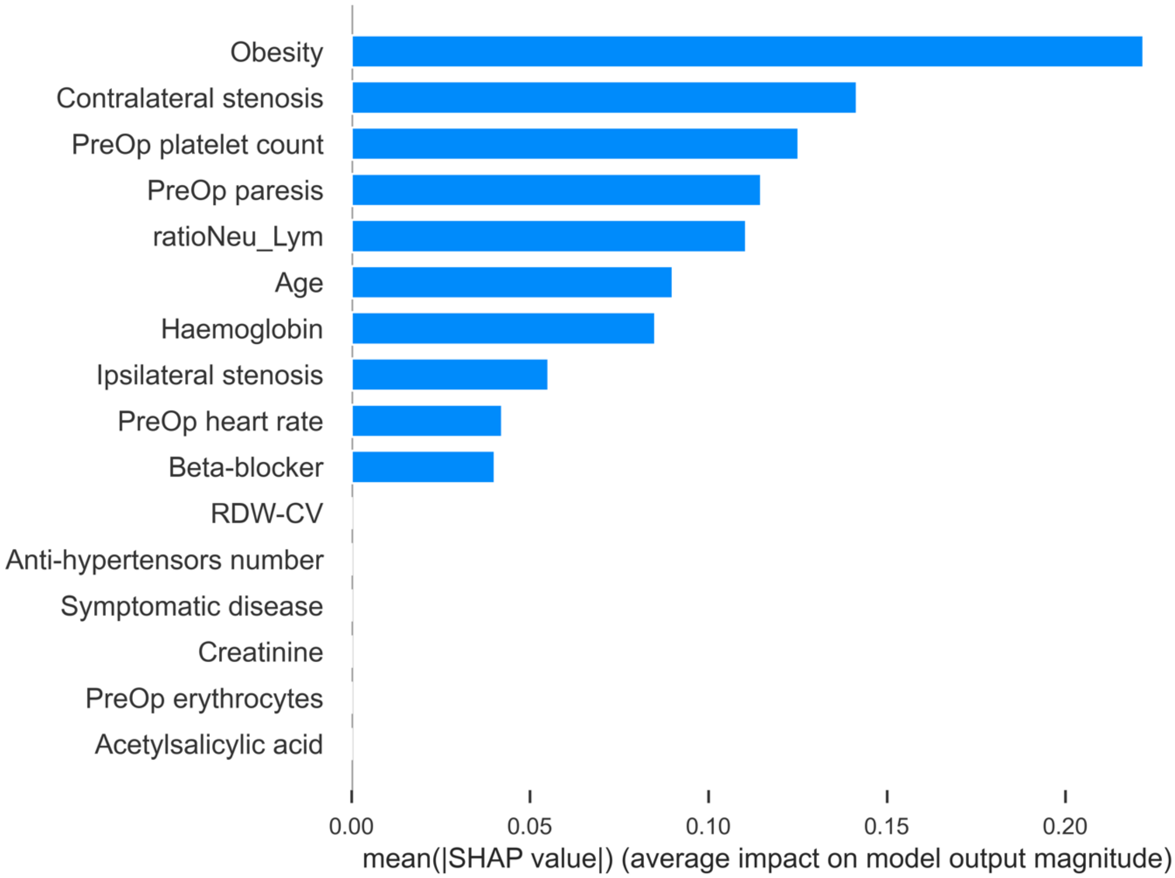
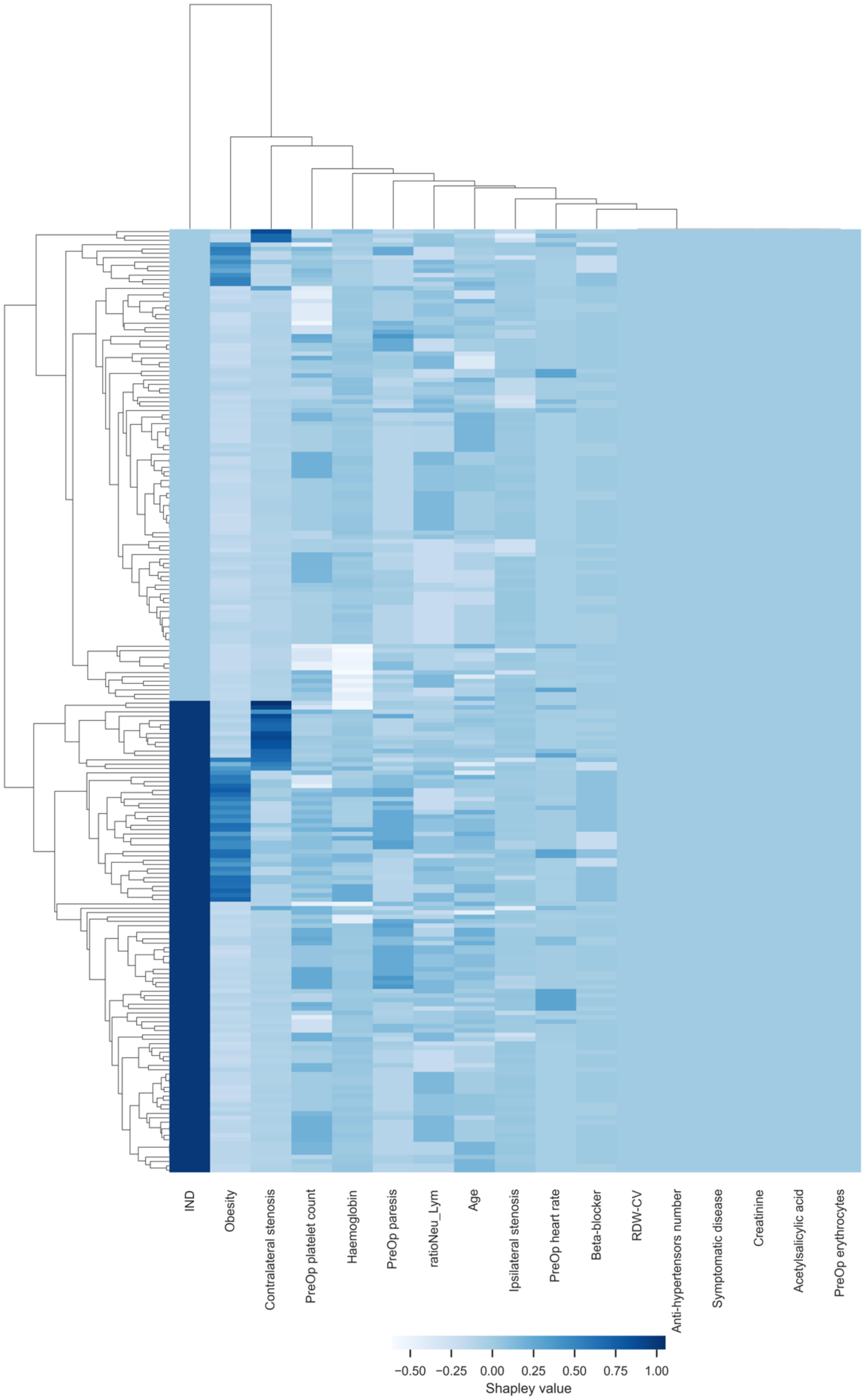

Obesity
Contralateral stenosis
PreOp platelet count
PreOp paresis
ratioNeu_Lym
Age
Haemoglobin
Ipsilateral stenosis
PreOp heart rate
Beta-blocker
RDW-CV
Anti-hypertensors number
Symptomatic disease
Creatinine
PreOp erythrocytes
Acetylsalicylic acid
−0.50
−0.25
0.00
0.25
0.50
0.75
1.00
SHAP value (impact on model output)
High
Feature value
Low

Figure 4



Obesity
Contralateral stenosis
PreOp platelet count
PreOp paresis
ratioNeu_Lym
Age
Haemoglobin
Ipsilateral stenosis
PreOp heart rate
Beta-blocker
RDW-CV
Anti-hypertensors number
Symptomatic disease
Creatinine
PreOp erythrocytes
Acetylsalicylic acid
0.00
0.05
0.10
0.15
0.20
mean(|SHAP value|) (average impact on model output magnitude)

Figure 5


IND
Obesity
Contralateral stenosis
PreOp platelet count
Haemoglobin
PreOp paresis
ratioNeu_Lym
Age
Ipsilateral stenosis
PreOp heart rate
Beta-blocker
RDW-CV
Anti-hypertensors number
Symptomatic disease
Creatinine
Acetylsalicylic acid
PreOp erythrocytes
−0.50 −0.25 0.00 0.25 0.50 0.75 1.00
Shapley value