Clinical significance and early detection of large vessel occlusion in acute ischemic stroke

PhD Thesis

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1. Introduction

Acute stroke is a leading cause of death and one of the most common causes of permanent disability. In our country, around 26,000 acute stroke cases occur each year, placing a significant burden on both healthcare and society. The vast majority of stroke cases (around 80%) are acute ischaemic strokes (AIS), in which brain damage and neuronal death occur due to local ischaemia. The outstanding circulatory demand of the brain and thus its susceptibility to ischaemia is illustrated by the fact that approximately 15-20% of the total cardiac output enters the brain, despite a brain mass of only 2% of body weight. The cerebral blood supply is provided by 4 major arteries, which form a complex system of branches and collaterals around the brain tissue.

The etiology of AIS is diverse, it can be due to large vessel atherosclerosis, cardiogenic embolization, small vessel disease and several predisposing factors of thrombosis. Accordingly, the main risk factors for AIS are those pathologies that predispose to atherosclerosis or thrombus formation. Hypertension (HT), diabetes mellitus (DM), dyslipidaemia and atrial fibrillation (AF) are common diseases, and their presence increases the risk of developing AIS several-fold. Also, the predisposing role of increasing age, smoking and several hereditary diseases should be highlighted.

The clinical presentation of AIS is heterogeneous, with symptoms depending on the location of the affected brain area. In general, ischaemia of the anterior circulation (supply area of the middle cerebral artery (MCA) and anterior cerebral artery (ACA)) results in contralateral hemiparesis, homonymous hemianopia, speech impairment if the dominant hemisphere is affected and hemineglect if the non-dominant hemisphere. Posterior circulation (supply area of the veretbral arteries (VA), basilar artery (BA) and posterior cerebral arteries (PCA)) is affected, with syndromes characterised by brainstem, cerebellar and hemiparetic symptoms. Several stroke scales, such as the Cincinnati Prehospital Stroke Scale (CPSS) and the National Institutes of Health Stroke Scale (NIHSS), are being developed to help identify stroke symptoms and assess their severity.

During AIS, nearly 2 million nerve cells ruin every minute, so the primary goal of acute treatment is to restore cerebral circulation and achieve recanalization as soon as possible. Currently, the most widely used recanalization therapy is aiming pharmaceutical thrombus dissolution. Alteplase is the most commonly used agent for intravenous thrombolysis (IVT). However, it is important to note that IVT increases the risk of developing symptomatic

intracranial haemorrhage (sICH). A summary of the results of large clinical trials shows that the risks of IVT performed beyond 4.5 hours from symptom onset outweigh the expected benefits.

In some cases of AIS, the proximal parts of the cerebral vessels are occluded, resulting in so-called large blood vessel occlusions (LVO). In general, occlusions of the internal carotid artery (ICA), MCA M1, M2 and M3, ACA A1 and A2, VA, BA, and PCA P1 and P2 segments are considered as LVO, but there is considerable heterogeneity in the definitions used by different studies. In patients with LVO, IVT alone can achieve complete recanalization in only a minority of cases. Mechanical thrombectomy (MT) can be an effective therapeutic alternative, as over the last few years, several clinical trials have demonstrated that with modern endovascular devices the thrombi causing LVO can safely be removed, resulting in complete reperfusion and consequently good functional clinical outcomes.

Following the assessment of clinical symptoms, an accurate diagnosis of AIS can be obtained using imaging techniques. The use of CT has gained popularity due to its wider availability and ease of use. Native CT scanning can be used to distinguish ischaemic from haemorrhagic stroke and to assess early ischaemic signs up to a certain level. CT angiography (CTA) is the primary tool for detecting LVOs and for accurate assessment of collateral circulation. Perfusion measurements can be used to visualise the extent of irreversibly damaged and potentially compromised brain tissue.

It is important to note that for both IVT and MT, the sooner the intervention is started after the onset of symptoms, the greater the chance of achieving a good functional outcome. Therefore, the importance of early recognition of symptoms and organisation of patient pathways as quickly and smoothly as possible is paramount. Confirmation of suspected stroke and subsequent transport to the nearest stroke centre is the main focus of prehospital care. However, it should be highlighted that the vast majority of stroke centres are only accredited to perform IVT, known as primary stroke centres (PSCs). Due to the specific equipment and professional needs of MT, it can only be performed in comprehensive stroke centres (CSC), the number of which is limited.

AIS patients should be transported to the nearest stroke centre, usually a PSC, to start IVT as soon as possible. If an LVO is confirmed, a second ambulance transport is used to transfer the patient to a CSC to perform MT (referred to as drip-and-ship method in the literature). In this case IVT can be started as soon as possible, but in LVO cases this is only

moderately effective and the time from symptom onset to MT initiation may be increased significantly due to the transports. Another view is that patients with a very high probability of LVO should be transported to a CSC immediately so that MT can be started as early as possible (mothership approach), which may even compensate the effect of the slight delay in starting IVT. However, the application of this method requires the use of a prehospital tool that is easy to use and can accurately and reliably predict LVO cases.

2. Aims and methods

In the present thesis, 4 publications are presented, the primary aim of which was to investigate the suitability of currently available prehospital stroke diagnostic methods (mainly stroke scales) for the detection of LVO and to develop new LVO prediction methods. For all the presented work, data were extracted from the STAY ALIVE acute stroke registry (GINOP 2.3.2-15-2016-00048), which is a multicentre prospective data collection project with the participation of stroke centres of three Hungarian university hospitals (University of Debrecen, University of Szeged, University of Pécs). For all patients treated for AIS, detailed information was collected on anamnestic data, acute care parameters, imaging findings, information on recanalization interventions and outcomes. Primarily CTA was used to confirm the presence of LVO. According to Rennert et al. LVO was defined as the acute extra- and intracranial occlusions of the ICA, occlusions in the M1, M2 and M3 segments of the MCA, the A1 and A2 segments of the ACA, the VA, the BA, and the P1 and P2 segments of the PCA.

The accuracy of different stroke scales for LVO detection was investigated using receiver operating characteristic (ROC) analysis and sensitivity (SN) and specificity (SP) values were provided where appropriate. The relationship between individual variables or group of variables and the presence of LVO was assessed using logistic regression analysis. Finally, several machine learning methods were applied to determine the optimal combination of variables.

3. Results and discussing

3.1. Ability of stroke scales to detect large vessel occlusion in acute ischemic stroke

In our first study, we investigated the ability of a total of 14 commonly used stroke scales to detect LVO in AIS. In this study, we examined patients who were admitted to the stroke centre of University of Pécs within 4.5 hours after symptom onset.

A total of 180 patients (47.8% female) were included, 98 of whom had LVO (54.4%). Patients with LVO had significantly more severe symptoms compared to those without LVO (NIHSS 13 vs 6 points; P<0.001) The prevalence of PF was significantly higher, while the prevalence of DM was lower in the group of LVO patients (35.3% vs 17.1%; P=0.009 and 20.0% vs 36.0%; P=0.024).

Based on the ROC analysis the area under the curve (AUC) was among the best for NIHSS (AUC: 0.830), modified NIHSS (0.831), sNIHSS-EMS (0.816), sNIHSS-8 (0.830), sNIHSS-5 (0.826), RACE (0.809) and FAST-ED (0.809) scales (Figure 1). A total of 6 scales were found to have thresholds with at least 80% SN and 50% SP. A threshold that provided at least 70% SN and 75% SP was identified for 5 scales (Table 1).

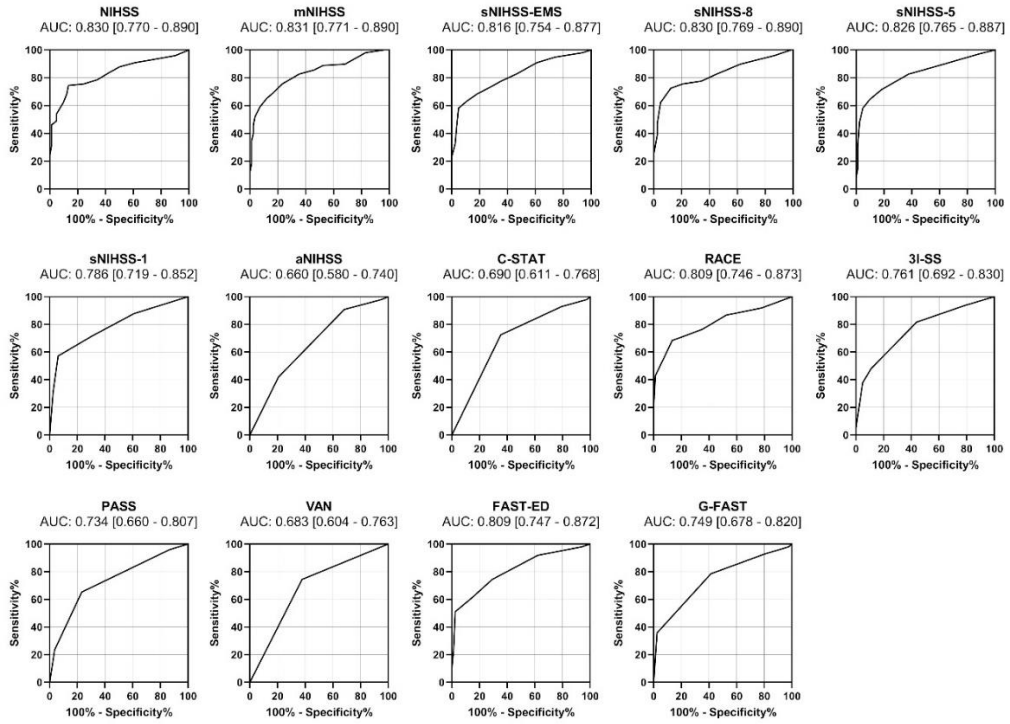

Figure 1. Receiver operating characteristic (ROC) curves analysing the ability of various stroke scales to discriminate large vessel occlusion in acute ischemic stroke: National Institutes of Health Stroke Scale (NIHSS), modified NIHSS (mNIHSS), shortened NIHSS for emergency medical services (sNIHSS-EMS), shortened NIHSS (sNIHSS), abbreviated NIHSS (aNIHSS), Cincinnati Stroke Triage Assessment Tool (C-STAT), Rapid Arterial Occlusion Evaluation (RACE), 3-Item Stroke Scale (3I-SS), Prehospital Acute Stroke Severity (PASS), Vision Aphasia Neglect (VAN), Field Assessment Stroke Triage for Emergency Destination(FAST-ED), Gaze Face Arm Speech Time (G-FAST). Area under the curve (AUC) values and 95% confidence interval are presented. The figure is the author's own work.

Table 1. Diagnostic accuracy of stroke scales according to different cut-off values

Stroke scale	Sensitivity (95% CI)	Specificity (95% CI)
Cut-off values with sensitivity ≥80% and specificity ≥50%		
NIHSS ≥6	87.8 (79.6-93.5)	50.0 (38.8-61.3)
mNIHSS ≥5	85.7 (77.2-92.0)	53.7 (42.3-64.8)
sNIHSS-EMS ≥5	82.7 (73.7-89.6)	53.7 (42.3-64.8)
sNIHSS-8 ≥4	82.7 (73.7-89.6)	54.9 (43.5-65.9)
sNIHSS-5 ≥3	82.7 (73.7-89.6)	62.2 (50.8-72.7)
3I-SS ≥2	81.6 (72.5-88.7)	56.1 (44.7-67.4)
Cut-off values with sensitivity ≥70% and specificity ≥75%		
NIHSS ≥9	75.5 (65.8-83.6)	75.6 (64.9-84.4)
mNIHSS ≥7	75.5 (65.8-83.6)	76.8 (66.2-85.4)
sNIHSS-8 ≥6	75.5(65.8-83.6)	79.3 (68.9-97.4)
sNIHSS-5 ≥4	71.4 (61.4-80.1)	81.7 (71.6-89.4)
RACE ≥4	71.4 (61.4-80.1)	78.1 (67.5-86.4)

Abbreviation: NIHSS, National Institutes of Health Stroke Scale; mNIHSS, modified NIHSS; sNIHSS-EMS, shortened NIHSS for emergency medical services; sNIHSS, shortened NIHSS; aNIHSS, abbreviated NIHSS; C-STAT, Cincinnati Stroke Triage Assessment Tool; RACE, Rapid Arterial Occlusion Evaluation scale; 3I-SS, 3-Item Stroke Scale; PASS, Prehospital Acute Stroke Severity scale; VAN, Vision Aphasia Neglect scale; FAST-ED, Field Assessment Stroke Triage for Emergency Destination scale; G-FAST, Gaze Face Arm Speech Time scale; LVO, large vessel occlusion.

Values are presented as percentages.

Based on our results, several stroke scales may be suitable for detecting LVO in AIS. Despite their outstanding accuracy, NIHSS and modified NIHSS are mainly suitable for in-hospital use, considering that their use requires professional experience and is time-consuming. However, it can be seen that shortes scales such as the sNIHSS-EMS, the sNIHSS-8, the sNIHSS-5, the RACE and 3I-SS scales also performed well for detecting LVOs. These scales are shorter, and their evaluation does not necessarily require routine, so their use may be feasible even in prehospital settings. However, as the results highlighted, none of the scales is able to achieve outstanding SN and SP simultaneously. Consequently, the threshold for LVO detection should be determined according to whether the primary aim is to reduce the number of false-positive or false-negative cases.

3.2. Detailed severity assessment of Cincinnati Prehospital Stroke Scale to detect large vessel occlusion in acute ischaemic stroke

The CPSS is a simple, three item stroke scale that is widely used by emergency services. It is easy and quick to learn and has a good ability to identify potential stroke cases. However, its ability to detect LVOs is limited. An important aspect is that the CPSS only tests for the

presence of three symptoms (facial paralysis, upper limb weakness and speech impairment), but not their severity. In our research, we investigated whether a detailed assessment of symptom severity would increase the accuracy of the CPSS for detecting LVOs. We created the detailed CPSS scale (d-CPSS) based on the severity scoring used in the NIHSS (Table 2).

Table 2. Detailed scoring of CPSS and d-CPSS compared to NIHSS scores

Severity of symptoms	CPSS	d-CPSS	NIHSS source item and score	
ARM			Item 5: arm motor drift	
No drift for 10 seconds	0	0	0	
Drift, but does not hit bed	1	1	1	
Some effort against gravity	1	2	2	
No effort against gravity	1	3	3	
No movement	1	4	4	
FACIAL PALSY			Item 4: facial palsy	
Normal symmetry	0	0	0	
Minor paralysis	1	1	1	
Partial paralysis	1	2	2	
Complete paralysis	1	3	3	
SPEECH			Item 9: aphasia	Item 10: dysarthria
Normal	0	0	0	0
Mild/moderate aphasia or dysarthria	1	1	1	1
Severe aphasia or dysarthria	1	2	2	2
Global aphasia or anarthic or mute	1	3	3	2
TOTAL	0 - 3	0 - 10		

Abbreviation: CPSS, Cincinnati Prehospital Stroke Scale; d-CPSS, detailed CPSS; NIHSS, National Institutes of Health Stroke Scale.

Data from a total of 421 AIS patients (48.7% female) with symptom onset within 6 hours were analysed, 183 (43.5%) were confirmed to have LVO. Admission CPSS, d-CPSS and NIHSS scores were significantly higher in patients with confirmed LVO (median score: 3 vs 2; 5 vs 3; and 11 vs 6 points; $P<0.001$ respectively). Upper limb weakness (92.3% vs 71.8%; $P<0.001$) and facial paralysis (85.8% vs 69.8%; $P<0.001$) were more common in patients with LVO, but there was no significant difference in the prevalence of speech impairment between the groups (77.0% vs 74.5%; $P=0.408$).

The associations between symptom severity and the likelihood of having an LVO were significant in all three cases after adjusting for potential confounders (odds ratio per 1 point increase: 2.045 [upper limb weakness], 2.133 [facial palsy], 2.299 [speech disturbance]; $P<0.001$ respectively). Using the ROC analysis, the AUC value of d-CPSS was significantly higher compared to the CPSS AUC value (0.788 vs 0.633; $P<0.001$). The AUC value of NIHSS

was found to be 0.795, which was not significantly different from the d-CPSS value (P=0.510). The ROC curves are shown in Figure 2. The optimal thresholds to discriminate an LVO were CPSS=3 (SN: 64.5%, SP: 58.4%), d-CPSS≥5 (SN: 69.9%, SP: 75.2%) and NIHSS≥11 (SN: 64.5%, SP: 87.0%).

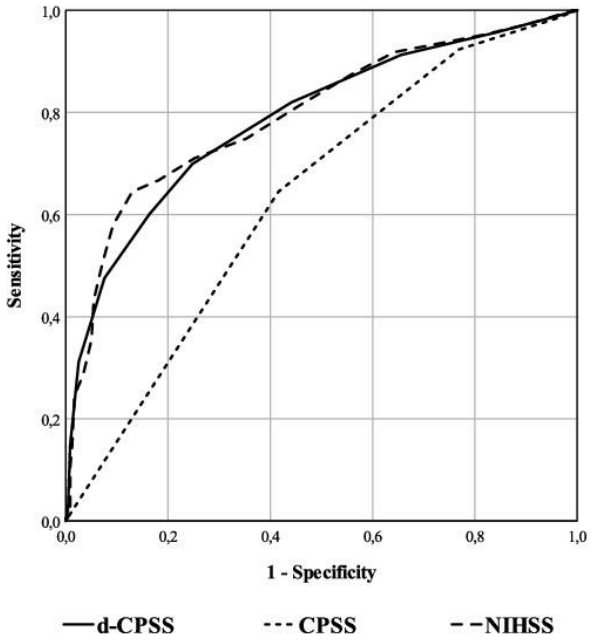

Figure 2. Receiver operating characteristic curves describing the capability of investigated scales to confirm a large vessel occlusion in acute ischemic stroke: Cincinnati Prehospital Stroke Scale (CPSS), detailed CPSS (d-CPSS) and National Institutes of Health Stroke Scale (NIHSS). The figure is the author's own work.

Our results showed that the NIHSS performs significantly better than the CPSS in detecting cases of LVO. The NIHSS is considered the gold-standard method for stroke severity assessment, but as mentioned earlier, its use requires experience and its evaluation is time-consuming, hence it is not commonly used prehospitally. The CPSS, widely used for education of lay people and by paramedics, is not sufficiently accurate for predicting LVOs, as our results confirmed. However, our research has highlighted that the detailed severity assessment of symptoms in the CPSS can significantly increase the LVO detection ability of this scale. The discriminative ability of d-CPSS approaches the accuracy of NIHSS. An additional advantage of the d-CPSS may be that it can be learned quickly and takes little time to assess.

3.3. Relationship between leukocyte counts and large vessel occlusion in acute ischemic stroke

In recent years, there have been many studies to identify biomarkers that can be used to distinguish between different types of strokes. However, a marker clearly suitable for the

detection of LVO has not yet been identified. Secondary neuroinflammation plays an important role in the pathogenesis of AIS. Ischemic brain injury triggers a systemic inflammatory response and induces a time-dependent activation of peripheral immune cells. A correlation between higher leukocyte count (especially neutrophil count) and stroke severity and infarct size has been demonstrated. Considering that in the presence of LVO extensive areas of the brain are affected and that in these cases the symptoms are usually more severe, we hypothesised that an association between the magnitude of the peripheral inflammatory response and the presence of LVO could be demonstrated.

A total of 419 patients (43.9% female) with symptom onset within 4.5 hours were included in our study, 167 (39.9%) were confirmed to have LVO. We recorded higher total white blood cell (WBC) counts in patients with LVO than in those without LVO ($9.27x10^9$/L vs $7.61x10^9$/L; P<0.001). Regarding leukocyte subtypes the median neutrophil count was significantly higher in the LVO group ($6.05x10^9$/L vs $4.69x10^9$/L; P<0.001). In contrast, no significant differences were observed between the groups for the other subtypes (Figure 3). The neutrophil/lymphocyte ratio was slightly higher in patients with LVO (2.83 vs 2.56; P=0.034). After adjusting for potential confounding factors, independent associations between total WBC count, neutrophil, lymphocyte and basophil count and the likelihood of LVO were demonstrated (Table 3).

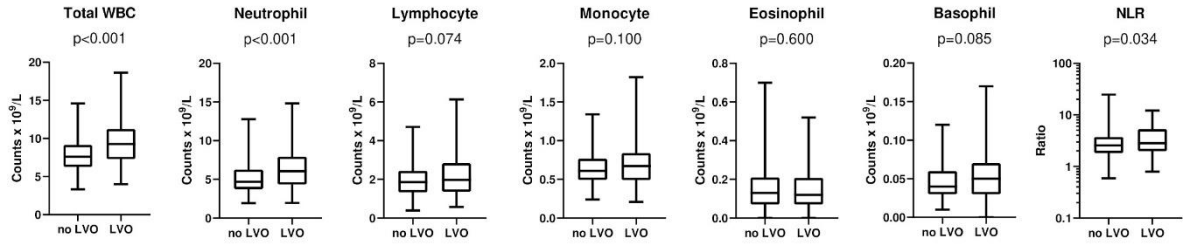

Figure 11. Comparison of admission total white blood cell (WBC) counts, leukocyte subtype counts and neutrophil-to-lymphocyte ratio (NLR) values in acute ischemic stroke according to the presence of large vessel occlusion (LVO). Boxes, 25% to 75% interquartile range; central horizontal bars, median; outer horizontal bars, minimum and maximum values. Statistics: Mann-Whitney *U* test. The figure is the author's own work.

Based on the ROC analysis, total WBC (AUC: 0.667; P<0.001) and neutrophil leukocyte count (AUC: 0.655; P<0.001) were proved to be moderately able to discriminate LVO cases. Marginally significant ability was demonstrated for neutrophil/lymphocyte ratios (AUC: 0.563; P=0.030). Interestingly, the median admission WBC values and neutrophil counts were significantly higher in patients with posterior territory LVOs compared to those with

anterior circulation area LVO ($8.77x10^9$/L vs $10.46x10^9$/L; P=0.005 and $5.89x10^9$/L vs $7.06x10^9$/L; P=0.001, respectively).

Table 3. Associations between leukocyte counts and the presence of large vessel occlusion in acute ischemic stroke

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Total WBC ($1x10^9$/L increase)	1.292 (1.187 to 1.405)	<0.001	1.405 (1.209 to 1.632)	<0.001
Neutrophil ($1x10^9$/L increase)	1.296 (1.181 to 1.421)	<0.001	1.344 (1.155 to 1.564)	<0.001
Lymphocyte ($1x10^9$/L increase)	1.321 (1.064 to 1.641)	0.012	1.631 (1.106 to 2.407)	0.014
Monocyte ($0.1x10^9$/L increase)	1.112 (1.018 to 1.214)	0.018	1.048 (0.903 to 1.217)	0.535
Eosinophil ($0.1x10^9$/L increase)	0.955 (0.807 to 1.131)	0.596	1.043 (0.799 to 1.363)	0.755
Basophil ($0.01x10^9$/L increase)	1.106 (1.024 to 1.194)	0.010	1.296 (1.119 to 1.501)	<0.001

Abbreviation: OR, odds ratio; CI, confidence interval; WBC, white blood cell; L, litre.
* Adjusted to sex, on admission NIHSS score, systolic blood pressure, diastolic blood pressure, body temperature, INR value, the presence of diabetes mellitus, atrial fibrillation, chronic heart failure, previous stroke/TIA, malignancy in patient history and anticoagulant or antidiabetic therapy at stroke onset.

The main finding of our study is that leukocyte counts (in particular total FVS and neutrophil counts) are associated with the likelihood of the presence of LVO in the early phase of AIS. Compared to patients without LVO, higher total WBC and neutrophil counts were detected in LVO cases already in the first hours after stroke onset. This highlights the role of systemic inflammatory mechanisms and their rapid activation after ischemic brain injury. Although leukocyte counts alone are not sufficiently accurate to reliably detect cases of LVO, the observed correlations highlight that neuroinflammatory markers may be a promising direction to find LVO detection biomarkers.

3.4. Optimization of large vessel occlusion detection in acute ischemic stroke using machine learning methods

The vast majority of currently available stroke scales only assess neurological symptoms and do not include other variables. However, several studies and our own results have confirmed that certain anamnestic data (e.g. the presence of AF), vital parameters (e.g. systolic blood pressure value) and some biomarkers have good predictive value. The aim of this study was to comprehensively investigate the association between several clinical variables and the

presence of LVO and to determine the most optimal combination of variables for LVO detection using machine learning methods.

A total of 526 patients (46.2% female) were enrolled (symptom onset within 4.5 h), the presence of LVO was confirmed in 227 cases (43.2%). 41 clinical parameters were recorded for each patient according to 4 groups: anamnestic/demographic data, vital parameters, laboratory values, symptom variables. When examining the variables individually, a total of 8 non-symptomatic parameters showed significant differences between groups according to the presence of LVO: admission NIHSS score (median 12 vs 6 points; P<0.001), systolic blood pressure (median 160 vs 169.5 mmHg; P=0.005), diastolic blood pressure (86 vs 90 mm Hg; P=0.034), INR (1.03 vs 1.00; P<0.001), total WBC count ($8.62x10^9$/L vs 7.94 $x10^9$/L; P=0.005), haemoglobin level (138 vs 141 g/dL; P=0.005), history of AF (35.8% vs 17.5%; P<0.001), and presence chronic heart failure (17.9% vs 8.9%; P=0.002). Regarding symptom variables (assessed using the NIHSS), only dysarthria and hemihypasthesia showed no significant difference between groups, all other symptoms were significantly more frequent and significantly more severe in the LVO group.

After pre-screening the data, the least absolute shrinkage and selection operator (LASSO) regression method was applied for feature selection. Using this method, a total of 9 variables were selected: aphasia, facial palsy, level of consciousness, visual field loss, gaze palsy, upper limb weakness, history of AF, known chronic heart failure, total WBC count. Using the selected variables, four machine learning methods were tested (random forest (RF), logistic regression (LR), elastic net method (ENM) and simple neural network (SNN)). A 10-fold cross-validation was used to validate the performance of the models. The obtained AUC values for the hold-out set and after 10-fold cross-validation were 0.986 and 0.736 for the RF model, 0.816 and 0.775 for LR, 0.813 and 0.773 for ENM and 0.808 and 0.772 for SNN. The AUC of NIHSS was 0.783 and 0.790 after cross-validation (P<0.001).

Our results show that the analysis of symptoms may provide the most information for detecting LVOs, but other non-symptomatic variables may also play an important role in the development of complex LVO detection methods. The presence of AF and chronic heart failure can be easily detected even prehospitally, but the measurement of WBC count is not yet possible. A noteworthy result is that the performance of the models optimized by machine learning methods was comparable to, but not significantly better than, that of NIHSS. This may suggest that the variables we considered are not sufficiently LVO specific. The observed

associations do not confirm a causal relationship and they may be modified by a number of unknown confounding factors unknown. Consequently, there is a need to identify more LVO specific variables, in particular biomarkers. Machine learning methods are playing an increasing role in the construction of optimised diagnostic models, but their application requires large amounts of data (big data). Stroke registries may play a key role in the creation of such databases.

4. Summary, conclusions

Our findings have shown that several stroke scales can be used to detect cases of LVO. These may even play an important role in determining prehospital pathways. However, it is important to note, that the most accurate scales require experience and are time-consuming to perform, and therefore cannot be used routinely in emergency care. Conversely, simpler scales optimised for prehospital use have lower performance, requiring a trade-off between good sensitivity and good specificity. To resolve this issue, a promising direction can be to assess the severity symptoms assessed by simple stroke scales in detail. Our results suggest that examining the symptoms assessed by the CPSS at the level of detail of the NIHSS yields a scale with a performance approaching that of the NIHSS. In addition, the identification of LVO specific variables and markers and the construction of complex LVO detection models using machine learning methods may play an important role in future studies. In our case, we have demonstrated an association between WBC counts, the presence of two common diseases (AF and chronic heart failure) and the presence of LVO.

Scientometrics

Scientific papers:

- Total: 9
- English-language: 7

Cummulative impact factor: 19.574 (based on the 2021 Journal Citation Reports™)

Publications related to the present thesis (cummulttive impact factor: 8.837)

1. Tárkányi G, Karádi ZN, Csécsei P, et al. Capability of stroke scales to detect large vessel occlusion in acute ischemic stroke - a pilot study. Stroke-skálák képessége nagyérelzáródás detektálására akut ischaemiás stroke-ban – pilot vizsgálat. Ideggyogy Sz. 2021;74(3-4):99-103. doi:10.18071/isz.74.0099 **IF:0.427**
2. Tarkanyi G, Csecsei P, Szegedi I, et al. Detailed severity assessment of Cincinnati Prehospital Stroke Scale to detect large vessel occlusion in acute ischemic stroke. BMC Emerg Med. 2020;20(1):64. Published 2020 Aug 24. doi:10.1186/s12873-020-00360-9 **IF: 2.119**
3. Tarkanyi G, Karadi ZN, Szabo Z, Szegedi I, Csiba L, Szapary L. Relationship between leukocyte counts and large vessel occlusion in acute ischemic stroke. BMC Neurol. 2020;20(1):440. Published 2020 Dec 4. doi:10.1186/s12883-020-02017-3 **IF: 2.474**
4. Tarkanyi G, Tenyi A, Hollos R, Kalmar PJ, Szapary L. Optimization of Large Vessel Occlusion Detection in Acute Ischemic Stroke Using Machine Learning Methods. Life (Basel). 2022;12(2):230. Published 2022 Feb 3. doi:10.3390/life12020230 **IF:3.817**

Other publications

5. Csecsei P, Tarkanyi G, Bosnyak E, et al. Risk analysis of post-procedural intracranial hemorrhage based on STAY ALIVE Acute Stroke Registry. J Stroke Cerebrovasc Dis. 2020;29(7):104851. doi:10.1016/j.jstrokecerebrovasdis.2020.104851 **IF: 2.136**
6. Kalmár JP, Tárkányi G, Karádi NZ, et al. A mechanikus thrombectomiát megelőző intravénás thrombolysis szerepe az akut agyi nagyérelzáródások kezelésében [The role of intravenous thrombolysis before mechanical thrombectomy in the treatment of large vessel occlusion strokes]. Ideggyogy Sz. 2022;75(1-02):23-29. doi:10.18071/isz.75.0023 **IF: 0.427**
7. Kalmar PJ, Tarkanyi G, Nagy CB, et al. Comparing Endovascular Treatment Methods in Acute Ischemic Stroke Due to Tandem Occlusion Focusing on Clinical Aspects. Life (Basel). 2021;11(5):458. Published 2021 May 20. doi:10.3390/life11050458 **IF: 3.817**
8. Bogner P, Chadaide Z, Lenzsér G, et al. Stroke-ellátást támogató teleradiológiai hálózat a Nyugat- és Dél-Dunántúlon [Teleradiology-based stroke network in Western and Southern Transdanubia in Hungary]. Orv Hetil. 2021;162(17):668-675. Published 2021 Apr 10. doi:10.1556/650.2021.32097 **IF: 0.497**
9. Kalmar PJ, Tarkanyi G, Karadi ZN, Szapary L, Bosnyak E. The Impact of Diabetes Mellitus and Admission Hyperglycemia on Clinical Outcomes after Recanalization Therapies for Acute Ischemic Stroke: STAY ALIVE National Prospective Registry. Life. 2022; 12(5):632. Published 2022 Apr 25. doi.10.3390/life12050632 **IF:3.817**

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