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PAPER

Machine learning for triage of strokes with large vessel occlusion using photoplethysmography biomarkers

Márton Á Goda[1,2,*], Helen Badge[3], Jasmeen Khan[3], Yosef Solewicz[2], Moran Davoodi[2], Rumbidzai Teramayi[3], Dennis Cordato[3], Longting Lin[3], Lauren Christie[3], Christopher Blair[3], Gagan Sharma[3], Mark Parsons[3] and Joachim A Behar[2]

[1] Pázmány Péter Catholic University Faculty of Information Technology and Bionics, Práter u. 50/A, Budapest 1083, Hungary
[2] Faculty of Biomedical Engineering, Technion Institute of Technology, Technion-IIT, Haifa 32000, Israel
[3] Ingham Institute for Applied Medical Research, Sydney Brain Center UNSW, Liverpool Hospital, Sydney 2052, Australia
[*] Author to whom any correspondence should be addressed.

E-mail: goda.marton.aron@itk.ppke.hu

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Abstract

Objective. Large vessel occlusion (LVO) stroke presents a major challenge in clinical practice due to the potential for poor outcomes with delayed treatment. Treatment for LVO involves highly specialized care, in particular endovascular thrombectomy, and is available only at certain hospitals. Therefore, prehospital identification of LVO by emergency ambulance services, can be critical for triaging LVO stroke patients directly to a hospital with access to endovascular therapy. Clinical scores exist to help distinguish LVO from less severe strokes, but they are based on a series of examinations that can be time-consuming and may be impractical for patients with dementia or those who cannot follow commands due to their stroke. There is a need for a fast and reliable method to aid in the early identification of LVO. In this study, our objective was to assess the feasibility of using 30 s photoplethysmography (PPG) recording to assist in recognizing LVO stroke. *Approach.* A total of 88 patients, including 25 with LVO, 27 with stroke mimic (SM), and 36 non-LVO stroke patients (NL), were recorded at the Liverpool Hospital emergency department in Sydney, Australia. Demographics (age, sex), as well as morphological features and beating rate variability measures, were extracted from the PPG. A binary classification approach was employed to differentiate between LVO stroke and NL + SM (NL.SM). A 2:1 train-test split was stratified and repeated randomly across 100 iterations. *Main results.* The best model achieved a median test set area under the receiver operating characteristic curve of 0.77 (0.71–0.82). *Significance.* Our study demonstrates the potential of utilizing a 30 s PPG recording for identifying LVO stroke.

1. Introduction

Stroke is the fifth leading cause of adult disability in the developed world (Guzik and Bushnell 2017). Acute stroke is a medical emergency, especially in stroke caused by large vessel occlusions (LVO) (Murray 2020). LVOs obstruct major cerebral arteries, and the decreased blood flow causes substantial brain damage and high rates of death and severe disability (Hendrix *et al* 2019, Krishnan *et al* 2021). Time-critical hyperacute LVO stroke treatments to restore cerebral blood flow, include mechanical (endovascular) thrombectomy and intravenous thrombolysis. Unfortunately, thrombolysis is not effective at quickly clearing large clots, but endovascular thrombectomy is, and hence substantially reduces long-term, stroke disability (Li *et al* 2023). These benefits are time-dependent, with faster access to treatment associated with better outcomes (Sheth *et al* 2015). However, there are often delays in the treatment that lead to poor outcomes (Lachkhem *et al* 2018).

Rapid early diagnosis of LVO stroke is the goal so that patients with LVO stroke are taken directly to thrombectomycapable hospitals, and those with non-LVO stroke (NL) and stroke mimics (SM) that can be taken to the closest hospital, and not 'overload' the comprehensive stroke centers. However, pre-hospital assessment of LVO stroke remains challenging due to limited diagnostic accuracy with existing clinical measures used to predict the likelihood of LVO (Krebs *et al* 2018, Smith *et al* 2018). The National Institutes of Health Stroke Scale (NIHSS) (Garcia-Esperon *et al* 2023) and Modified Rankin Scale serve distinct but complementary roles in the evaluation and management of LVO stroke (Goyal *et al* 2016). The NIHSS is an 11-item clinical assessment designed to assess clinical deficits and stroke severity quickly, it can be completed pre-hospital and before imaging can be completed (Smith *et al* 2018). However, the time taken to administer the full scale is prohibitive in a prehospital environment, so an abbreviated version, the 8-item Hunter-8, has been validated as a valid and feasible measure for prehospital rapid assessment. Apart from limited specificity for diagnosing LVO vs NL or SM, another limitation of the various NIHSS Scores is that they cannot accurately be performed with patients with significant cognitive or communication impairments. The NIHSS detects LVO strokes with sensitivity ranging from 73% at a threshold of ⩾10%–87% at ⩾6, with corresponding specificity from 74% to 52%. Lower thresholds like ⩾6 increase sensitivity but reduce specificity, while higher thresholds like ⩾10 or ⩾11 improve specificity at the cost of sensitivity (Smith *et al* 2018). The area under the receiver operating characteristic curve (AUROC) for identifying LVO using the Hunter 8 was 0.73 (95% CI 0.66–0.79) (Garcia-Esperon *et al* 2023). The limitations of these tools highlight the need for additional assessment methods for more accurate diagnosis of LVO stroke.

Strategies to enhance prehospital detection of LVO stroke include mobile stroke ambulances with qualified specialists and CT scanners onboard, that are effective at reducing delays to treatment. However, they are probably too expensive and resource-intensive for widespread implementation (Navi *et al* 2022). Increasing the diagnostic capability for stroke in all ambulances would have greater reach and impact. Thus, in the future, 'stroke-capable' ambulances might have the capability to use multi-modal data routinely collected by paramedics, including clinical data, NIHSS and bio-signals such as electrocardiogram (ECG) and photoplethysmography (PPG) (Choi *et al* 2021, Yu *et al* 2022). Emerging evidence shows the potential for physiological data to predict LVO stroke. The PPG signal is an optical measurement of the arterial pulse wave (Charlton *et al* 2019, 2023), generated when blood is ejected from the heart (Alastruey *et al* 2023). LVO markedly reduces cerebral perfusion and leads to significant changes in cerebral hemodynamics, including increased vascular resistance and alterations in pulse wave propagation (Derdeyn 2018, Silverman *et al* 2020, Kim *et al* 2021, Shimada *et al* 2023). These hemodynamic disturbances impair cerebral autoregulatory capacity and evoke compensatory sympathetic activation aimed at preserving cerebral blood flow. Through these mechanisms, LVO exerts systemic effects on central hemodynamics and autonomic cardiovascular control, which may manifest as subtle morphological (MOR) alterations in peripheral pulse waveforms (Luisi *et al* 2024).

The PPG signal can be obtained quickly using single-lead sensors with devices available on all ambulances. Based on the regulation of sympathetic and parasympathetic cardiovascular functions by the brain de la (De La Cruz *et al* 2019), we hypothesize that data-driven algorithms, trained using continuous raw PPG recordings, have the potential to detect structural changes indicative of stroke of LVO etiology. Furthermore, cardiac dysfunction can result from various neurologic injuries, including stroke and spinal cord injury (Hu *et al* 2023). Previous research has demonstrated the potential for using machine learning (ML) to predict LVO stroke based on physiological data. Accordingly, the main goal of this research is to evaluate the feasibility of triaging LVO stroke using a short-PPG recording (30 s long). Figure 1 presents a graphical abstract summarizing the main aspects of the study. Such a technology would enable rapid patient triage in 'stroke smart ambulance' emergency services.

2. Materials and methods

2.1. Dataset

The study protocol received approval from the South West Sydney Human Ethics Committee (2019/ETH00096 number). This study was performed in accordance with the declaration of Helsinki. All adult participants provided written informed consent for publishing identifying details in this study. The data were collected at Liverpool Hospital in Sydney, and measurements were taken in the emergency department and/or the Neurophysiology Department, in stable patients. These patients were acute hospital presentations with acute stroke and/or stroke symptoms. These patients were acute hospital presentations with acute stroke and/or stroke symptoms. The fingertip PPG signals were recorded using a PowerLab 16/35 data acquisition system with a Bio Amp (FE231) and the manufacturer's fingertip PPG transducer (ADInstruments, Bella Vista, NSW, Australia). This transmission-type fingertip sensor typically produces stronger pulsatile (AC) components than reflective sensors. The setup provides high-quality

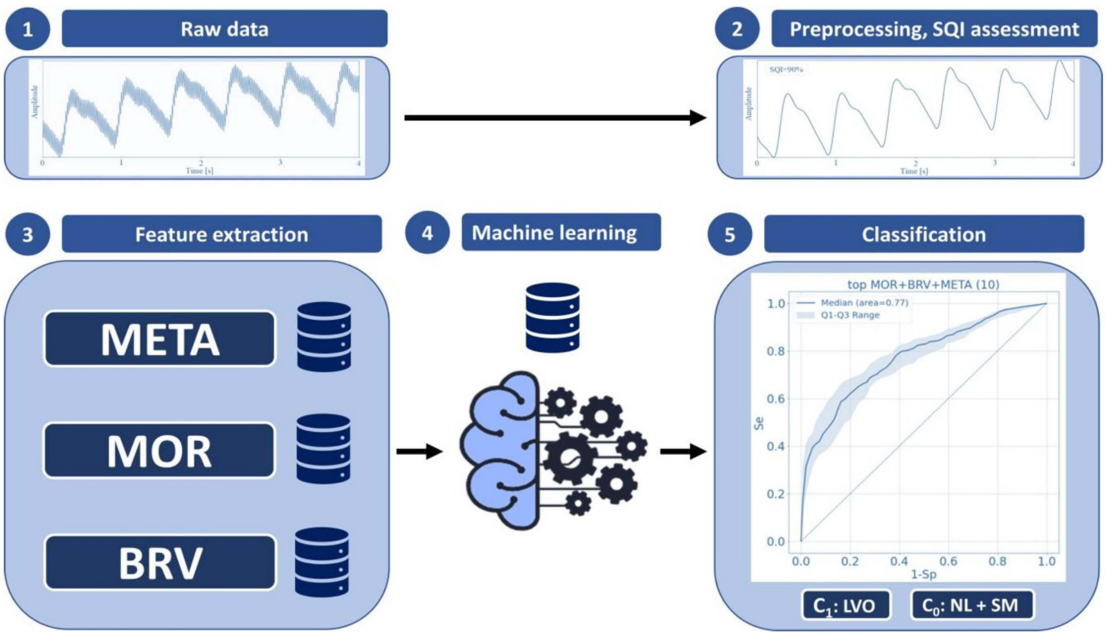

Figure 1. Graphical abstract. First, the process begins with raw PPG extraction. The second step is preprocessing, which includes filtering and signal quality assessment. In the third step, features are extracted, including META features (age, sex), PPG morphological features (MOR), and beat rate variability (BRV). Fourth is the evaluation of feature importance, a machine learning-based model is trained and validated. Finally, in the fifth step, the triage of LVO stroke is tested and evaluated using the area under the receiver-operating characteristic curve (AUROC). LVO: large vessel occlusion stroke. NL.SM: non-LVO stroke + stroke mimics.

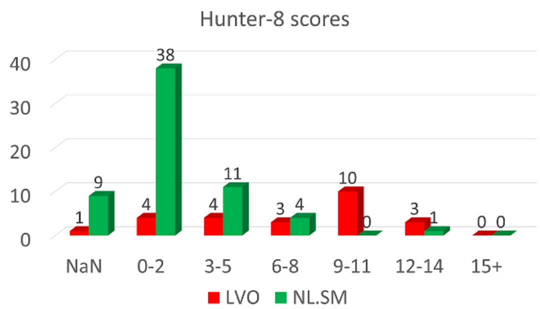

Figure 2. Distribution of Hunter-8 scores. LVO: Large vessel occlusion stroke. NL.SM: non-LVO stroke + stroke mimics.

PPG signals through the Bio Amp's low-noise input, 1 kHz sampling rate, 16-bit resolution, and built-in filtering (0.1 Hz high-pass, 45 Hz low-pass), ensuring stable and detailed waveform recordings. The amplitude range was ±100 mV. The PPG sensors were placed on the left ear lobe and either on the left index finger or on the left middle finger. The finger pulse signal and the earlobe signal were measured at 5 V. Only fingertip PPG recordings were used for the analysis.

Figure 2 illustrates the distribution of Hunter-8 scores across predefined score intervals for LVO and LVO-mimic (SM)/non-strokes (NS) patients. Positive recordings for LVO (25 recordings) were classified as the positive class denoted as C_1, while the remaining 61 recordings, including SM and NS, comprised the negative class denoted as C_0 (see figure 3 panel (A)). SM presents an acute onset of focal neurological symptoms but is later diagnosed as having a non-vascular origin.

The median duration of recordings was 10 min (interquartile range: 10–10 min). The median age of the whole cohort was 69.5 years (interquartile range: 61–77.3, see figure 3 panel (B), and 65% of the participants were male. The median BMI was 27.5 (interquartile range: 24.4–31.1), with 13 patients lacking BMI data. Notably, approximately 60% of the patients were either overweight or obese. The recordings were segmented into 30 s windows, and each window was used as an example for training or testing. The choice of a 30 s window length represents a practical trade-off, long enough to capture relevant signal variability, yet short enough to enable prompt decision support.

PPG signals were recorded in a hospital setting. No patients were excluded based on any cardiac abnormalities. This decision was intentional, as the study aimed to assess the feasibility of the proposed

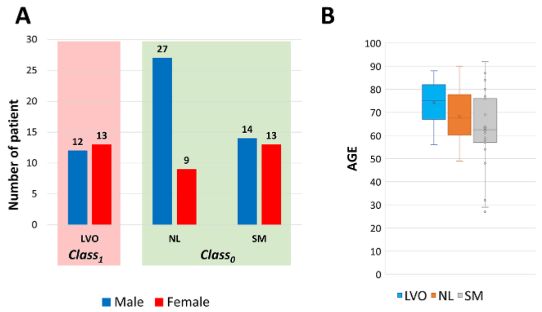

Figure 3. Sex panel (A) and age panel (B) distribution by stroke types. LVO: large vessel occlusion stroke. NL: non-LVO stroke. SM: stroke mimics. NL.SM stroke includes both NL and SM cases.

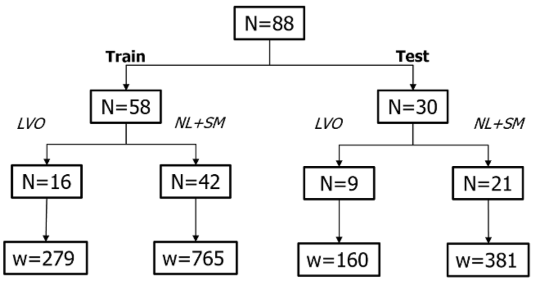

Figure 4. Workflow of the training and evaluation process: The process begins with data preparation, involving the segmentation of 30 s PPG intervals and feature extraction. The training and validation phases are conducted iteratively 100 times on randomly shuf-fled yet stratified datasets to maintain class balance. Finally, model evaluation is performed to assess and compare performance metrics.

method in a representative acute stroke population, including patients with common comorbidities that may influence PPG signal characteristics.

2.2. Preprocessing and feature extraction

The raw PPG time series were pre-processed to eliminate baseline wander and high-frequency noise. This involved employing a zero-phase fourth-order infinite impulse response bandpass filter, set within the range of 0.5–12 Hz. Each recording was segmented into 30 s windows, totaling 1801 windows for analysis. A total of 216 windows were excluded from the assessment because they were unsuitable for PPG signal quality index calculation, primarily due to significant amplitude modulation. There was no information leakage to maintain data integrity, ensuring that all recordings for a given patient were assigned exclusively to either the training or test set. The PPG MOR waveform features were extracted for each window using the *pyPPG* Python toolbox (Goda *et al* 2024), resulting in 101 MOR features. Additionally, beating rate variability (BRV) features were derived based on the variability between consecutive PPG beats, resulting in 17 BRV features. Two META features, age, and sex were also used. During the feature calculation, the 10 min recordings were divided into 30 s windows. For each MOR feature, the mean statistical descriptors were calculated within the 30 s window.

2.3. ML

The dataset was split into training and test sets, with the training set comprising 2/3 and the test set 1/3 of the entire dataset (see figure 4). This process was repeated 100 times with a random train-test split each time.

On average, 9 patients were selected for the test set and 16 for the training set in C_1. For C_0, on average, 21 patients were chosen for the test set, while the remaining 42 were used for training (see figure 5).

Three types of features were used: BRV, MOR, and META. Logistic regression models were trained when considering one of the feature types (i.e. BRV or MOR or META) and all feature types (BRV + MOR + META). This was done to evaluate the relative added value of each feature type. The top 10 features were selected based on their im- portance using recursive feature elimination. A total of 100 AUROC were computed from models using all four sets of features. Based on these AUROC values, the final results present the calculations of the median, 25th percentile, and 75th percentile.

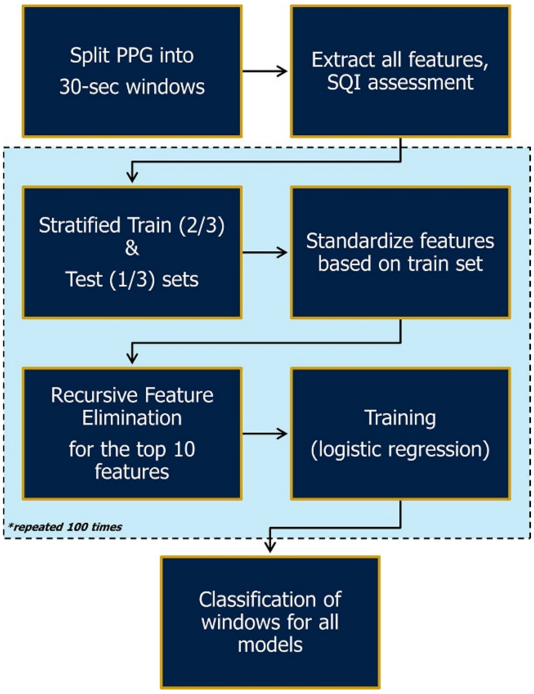

Figure 5. Classification of 88 patients. Patients' recordings (N) were divided into 30 s windows (w). The train and test sets are stratified following signal quality checks. LVO: large vessel occlusion stroke. NL: non-LVO stroke. SM: stroke mimics.

Table 1. Results of LVO stroke triage.

Features	Specificity	Sensitivity	Precision	$F1$-score	AUROC
MOR	65%	59%	55%	68%	0.66 (0.62–0.71)
BRV	57%	72%	59%	68%	0.69 (0.63–0.73)
META	41%	88%	59%	70%	0.71 (0.64–0.77)
ALL	66%	74%	62%	71%	0.77 (0.71–0.82)

2.4. Results

Our project involved 88 patients, including 25 LVO and 61 NL.SM cases. During training and validation, three types of features were used: META, MOR, and BRV. The best model utilized all feature types and achieved an AUROC of 0.77 (0.71–0.82) against 0.71 (0.64–0.77) for the best single modality model. For this model, the top 10 selected features were 1 META, 8 MOR, and 1 BRV.

Table 1 summarizes the results of the LVO stroke triage. Figure 6 presents the ROC curves for all the models. The following performance statistics were reported for the per-window classification task: the area under the ROC curve, precision, sensitivity, specificity, and $F1$ score.

In each iteration, the top 10 features were chosen for every trained model. To identify the most important features (across all trained models), we examined which features were most frequently selected among the top 10 across all 100 iterations. Specifically, the most frequently selected features are listed in table 2 (Charlot *et al* 2009, Goda *et al* 2024).

The top 5 features are presented in figure 7. This figure shows which features are most distinctive for the two classes. The diagonal plots represent the normalized distributions of each feature.

3. Discussion

This study demonstrated the potential of a novel data-driven approach using PPG signals to identify LVO stroke. The continuous physiological patient data recorded in the ambulance represents an opportunity for automated and fast stroke triage and could potentially support 'stroke-capable' ambulances in the future.

We trained a ML model using PPG biomarkers to develop this clinical decision support tool. This data-driven approach presents an alternative to clinical scores that take longer and may be impractical for patients with dementia or those who cannot follow commands.

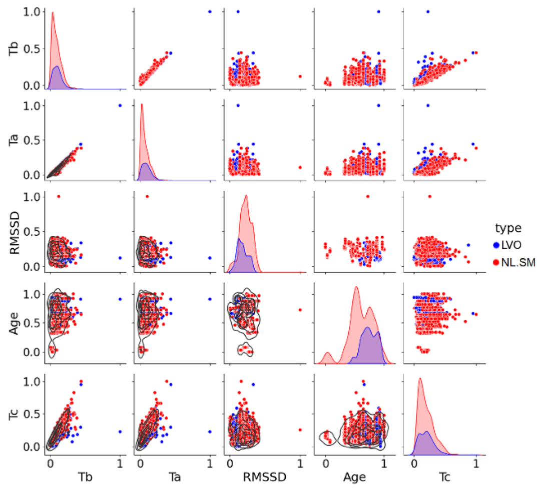

Figure 6. Receiver operating characteristic curves for the per-patient classification task and as evaluated on the test sets, with the median (curve) and interquartile range (envelope). The models presented in panels (A)–(C) are trained with one type of feature, i.e. morphological feature (MOR), beat rate variability (BRV), or patient information (META), respectively. The model presented in Panel D is trained with MOR, BRV, and META features. The red point represents the sensitivity-specificity (SE-SP) cutoff for the Hunter-8 score used in clinical practice. This point is evaluated for all patients who had a HUNTER-8 score documented in our cohort (76 out of 88 patients).

Table 2. Top 10 feature names, descriptions, types, and units.

Feature	Description	Type	Unit
Age	Age of the patient	META	s
T_a	a-point time, the time between the pulse onset and a-point	MOR	s
T_b	b-point time, the time between the pulse onset and b-point	MOR	s
T_c	c-point time, the time between the pulse onset and c-point	MOR	s
T_{dw25}/T_{sw25}	Ratio of the diastolic width vs. the systolic width at 25% width	MOR	%
RMSSD	The RMSSD measure over a segment of peak-to-peak time series.	BRV	nu
T_{b-d}	b-d time, the time between the b-point and d-point	MOR	s
A_{p2}/A_{p1}	Ratio of the p2-point amplitude vs. the p1-point amplitude	MOR	%
AI	The ratio of the height of the late systolic peak to that of the early systolic peak in the pulse	MOR	%
T_{pw75}/T_{pi}	Ratio of the pulse width at 75% of the systolic peak amplitude vs. the pulse interval	MOR	%

In 2024, Goda *et al* (2024) introduced a standardized *pyPPG* toolbox for PPG feature extraction. The extracted PPG-based and META features were used for the first time in LVO stroke stratification. The main contribution of our study is demonstrating the feasibility of identifying strokes using short-term (30 s) PPG signals. Our analysis of feature importance demonstrated that the PPG-based features have a high predictive value. The current results introduce a novel medical assessment method utilizing short-term PPG signals. This innovative approach enhances the capability of smart ambulances, enabling rapid evaluation of LVO-type stroke orientation during patient hospitalization.

The results obtained in this research are promising, indicating that data-driven based LVO stroke phenotyping holds significant potential for future applications using short-term (30 s) PPG recording. It is important to note that in our cohort, the HUNTER-8 demonstrates very high specificity ($\sim$0.96) but lower sensitivity ($\sim$0.57). The sensitivity is higher than previously published, as the current dataset has more LVO stroke than would be expected in a random sample of prehospital patients, as Liverpool Hospital is an endovascular center. Additionally, the Hunter-8 is unsuitable for patients who cannot

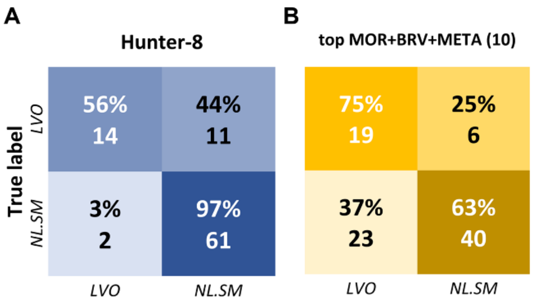

Figure 7. Distribution plots for the top 5 most significant features, with blue indicating LVO type stroke and red indicating NL.SM, including non-LVO stroke (NL) and stroke mimics (SM) cases.

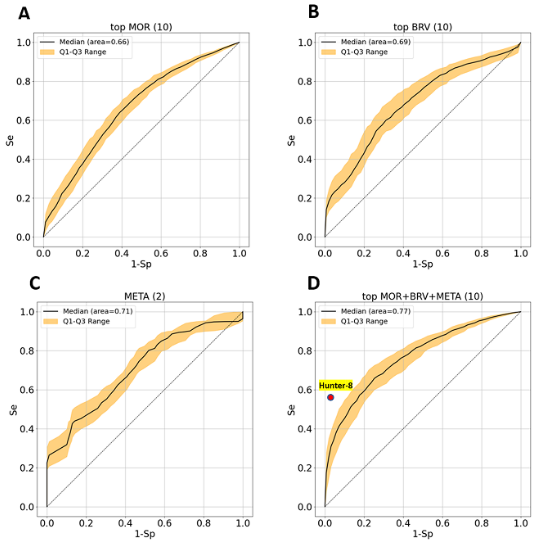

Figure 8. Confusion Matrix for Hunter-8 Evaluation panel (A) and machine learning model panel (B): this figure illustrates the classification performance of the Hunter-8 evaluation panel (A) and the machine learning model panel (B) against confirmed diagnoses. The trained model was built using the top 10 extracted features, including morphological features (MOR), beat rate variability (BRV), and patient metadata (META). The matrix highlights true positives, false positives, true negatives, and false negatives. Rows correspond to actual diagnoses, while columns represent predicted outcomes. LVO: large vessel occlusion stroke. NL.SM: non-LVO stroke + stroke mimics.

respond to questions. This was the case for 13% (12/88) of patients in this study, who had a missing HUNTER-8 score. The mean sensitivity (>0.74) of the trained model is significantly higher than that of the Hunter-8 score, suggesting potential short-term benefits for LVO stroke detection. Future research could explore using combined ECG data and whether multimodal clinical and physiological data will improve accurate diagnosis, along with AI-based voice, speech, and video recognition. Implementation studies to support integration into clinical practice will also be important.

The main limitation of this study is the small sample size.

To enhance the accuracy and relevance of LVO stroke stratification, it is crucial to increase the dataset size and incorporate data recorded from ambulances. Recruiting patients and performing the required clinical measurements in acute stroke settings is inherently challenging and time-consuming. Nevertheless, this work was designed as a proof-of-concept investigation to explore the feasibility of using PPG for rapid LVO-type stroke stratification. By including data captured during ambulance transport, the dataset will better reflect the patients' physiological status at the point of initial medical intervention. This approach can ensure a better understanding of patients' conditions as they are being taken by the ambulance, providing a clearer picture of their physiological state before they reach the emergency department. Further improvements may also be achieved using deep learning. Given the modest dataset size, we envisage the usage of a foundation model which would be fine-tuned to our downstream task.

Another limitation stems from the inherent dependence of transmissive PPG on the pulsatile component of arterial blood flow within the microvasculature. As arterial blood volume varies with each cardiac cycle, the balance between absorbed and transmitted light fluctuates accordingly, giving rise to the characteristic pulsatile PPG waveform that is synchronous with the heartbeat. Consequently, any factor that alters local perfusion or induces motion can interfere with this optical modulation, leading to signal distortion and reduced measurement fidelity.

This study emphasized the feasibility of using a data-driven approach leveraging a short 30 s PPG recording to triage LVO strokes. It encourages more research and clinical exploration in this area to develop future technologies and smarter ambulances. By understanding the significance of PPG data, we can improve emergency medical services and help patients receive faster and more accurate stroke care.

Data availability statement

The data cannot be made publicly available upon publication because they contain sensitive personal information. The data that support the findings of this study are available upon reasonable request from the authors.

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ORCID iDs

Márton Á Goda 0000-0003-0120-5940
Helen Badge 0000-0002-5351-393X
Jasmeen Khan 0009-0007-0555-620X
Yosef Solewicz 0000-0003-3987-1201
Moran Davoodi 0000-0001-6322-6523
Dennis Cordato 0000-0001-8447-6644
Longting Lin 0000-0001-7104-9846
Lauren Christie 0000-0003-4900-5614
Christopher Blair 0000-0001-8685-9622
Mark Parsons 0000-0001-8874-2487
Joachim A Behar 0000-0001-5956-7034

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