Improving the identification of large vessel occlusion stroke during the emergency call: a protocol of the LESTOR study

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Abstract

Background

Large vessel occlusions (LVO) cause up to 30% of acute ischemic strokes. Mechanical thrombectomy is the first line treatment performed by neurointerventionalists. In Germany, neurointerventionalists are mostly situated in comprehensive stroke centres (CSC). Thus, long transport distances to CSCs may be necessary. The aim of this study is to design, implement and evaluate an intervention that involves lay first responders (LFR) in the early identification of LVO, followed by a direct assignment to a CSC.

Methods

This controlled study with a stepped-wedge design and clustering of six emergency control centres in southwest Germany will stepwise implement LVO screening performed during the emergency call. Individuals with suspected LVO in both the control and intervention group (n=250) will undergo the usual treatment. In addition, emergency medical service dispatchers will screen patients in the intervention group for cortical stroke symptoms and refer those patients with suspected LVO to a CSC, either by ambulance or air rescue. The primary endpoint is the clinical outcome measured by the modified Rankin Scale 90 days post-stroke. In addition, we will perform a qualitative process evaluation.

Discussion

We will assess the feasibility and cost-effectiveness of a systematic screening for symptoms of LVO stroke implemented at the emergency control centre. The process evaluation will provide additional insight into how the participating emergency professionals perceive the intervention and the psychological impact on LFR.

Conclusions

We hypothesize that early, pre-hospital identification of LVO patients and an optimized rescue chain will enable earlier treatment - especially in rural areas. We expect improved clinical outcomes for LVO patients and a better understanding for future studies with larger sample sizes.

Trial registration

DRKS, DRKS-ID: DRKS00022152. Registered 19th October 2020, https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00022152; WHO UTN: U1111-1253-5758.

Background

Strokes are the second leading cause of death in adulthood worldwide, with an increasing tendency.[1–3] In 2017, strokes led to 75,861 deaths per year in Germany[1] and are one of the leading causes of long-term disability.[1,4,5] Around 30% of acute ischemic strokes are caused by the occlusion of large intracranial arteries (large vessel occlusion, LVO).[6] Systemic thrombolysis alone results in recanalisation in only 10-20% of these patients.[7] The more effective combination with mechanical thrombectomy (MT) is the treatment of choice for patients with LVO.[8] In Germany, however, MT is not ubiquitously available. Mostly, only comprehensive stroke centres (CSCs) can perform systemic thrombolysis and endovascular stroke therapy 24 hours per day, 7 days per week. As treatment is time-sensitive and the transport of LVO patients from a rural area to the next CSC can be lengthy, the delay from stroke onset to the beginning of MT reduces the chance of functional recovery (“time is brain”). [9,10]

The current practice of pre-hospital stroke care in Germany is mainly based on two concepts: the "drip-and-ship" and the "mothership" approach.[11,12] The majority of healthcare systems use the drip-and-ship concept, initially transporting all patients with suspected stroke to the nearest primary stroke centre. Thrombolysis is performed immediately after cerebrovascular imaging. Patients with an indication for thrombectomy are subsequently transferred to a CSC. In the mothership approach, an emergency team evaluates stroke symptoms on site. If the emergency team suspects stroke with LVO, it organises the admission to the closest hospital capable of MT. In rural areas far from a CSC, this may require a time-consuming secondary transport, e.g. via helicopter. To optimise pre-hospital stroke care and thereby shorten the time from symptom onset to treatment, the LESTOR approach aims at involving lay first responders (LFR) in the identification of LVO already during the emergency call.

Lay people were successfully involved in phone-assisted cardiopulmonary resuscitation[13] and the application of a tourniquet to stop the bleeding in arterial limb haemorrhage.[14] Previous studies investigated the feasibility of stroke identification by collaboration between

emergency medical service (EMS) dispatchers and LFR administering scales over the phone, such as the Cincinnati Pre-Hospital Stroke Scale (CPSS) or the Face-Arm-Speech-Time (FAST) screening tool.[15–17]

To accelerate the initiation of therapy, several studies adapted the transport of patients with suspected LVO strokes by applying pre-hospital identification tools such as the Rapid Arterial oCclusion Evaluation (RACE) scale,[18,19] the adopted Prehospital Acute Stroke Severity Scale (PASS),[20] and the modified Prehospital Acute Stroke Severity Scale (mPASS),[21] the FAST-PLUS test,[22] the Emergency Medical Stroke Assessment (EMSA)[23] or the Stockholm Stroke Triage System (SSTS).[24] These pre-hospital stroke identification tools are promising for LVO stroke recognition by EMS personnel,[18,25,11,24] but none of these studies includes LFR.

Based on existing LVO screening scores, the LESTOR study team derives a score aiming at the earliest possible identification of cortical symptoms suggestive of LVO stroke, during the emergency call. The team re-evaluates the LVO score in an artificial study setting with simulated patients and emergency calls, then prospectively revises and validates it in the real-life emergency setting (urban emergency district of Freiburg, Germany). Subsequently, all the emergency professionals (emergency doctors, dispatchers and other EMS staff) are trained on the administration of the LVO score. Recently published studies confirm that a high-quality implementation of a newly derived score is critical to its success[26] and depends on training and feedback of performance.[23] Therefore, we evaluate this training for its effectiveness.[27]

We will gradually implement the new approach into the emergency system in southwest Baden-Wuerttemberg, comprising emergency control centres, and air rescue operators. According to the LESTOR approach, when the screening indicates LVO, EMS dispatchers will alert air rescue in addition to an ambulance, if this happens to be the fastest transport option. Based on usual practice, in addition to the EMS personnel, a ground-based emergency doctor will also be sent simultaneously to the patient, where appropriate. The patient's symptoms will be re-evaluated upon arrival on site. Patients with suspected LVO stroke will be transported to a CSC as quickly as possible, by either air rescue or ambulance. If a non-LVO stroke is suspected, the patient will be transferred to the nearest primary stroke centre by ambulance.

Aim of the study

The main study objective is to implement and evaluate an intervention that involves LFR in the early identification of a stroke with LVO. The recognition of cortical symptoms suggestive of LVO by the EMS dispatcher during the emergency call is then expected to trigger a dispatch strategy optimised for the patient's fastest transport directly to a CSC. For this purpose, we will use a specifically designed LVO score (derived from published scores, specifically adapted to emergency calls via phone).

We hypothesise that the pre-hospital interval will be shortened and thus the intervention group (immediate admission to a CSC in the case LVO is suspected) will show a better clinical outcome compared to the control group (application of the sequential drip-and-ship approach or the mothership approach in LVO patients without LVO screening at the emergency control centre). The primary outcome is measured by the modified Rankin Scale (mRS) 90 days post-stroke.

We further hypothesise that the new approach will be beneficial in terms of cost effectiveness: although the costs of the rescue and primary care procedures might increase in the intervention group, the clinical outcome will generally improve, leading to a reduction in the treatment costs in the long-term.

Moreover, we attempt to gain insight into the professionals' perspective in terms of benefits, barriers and side effects. Finally, the impact of the emergency situation and the examination of stroke patients during the emergency call on LFR will be assessed.

Methods/design

Study design

The project is divided into three stages:

Stage 1: First, based on existing scores that have been successfully applied in previous studies,[28] we develop a dedicated LVO screening tool suitable for use during telephone calls in close collaboration with dispatchers at the emergency control centre. The identification of stroke patients as candidates for thrombectomy presenting a left-hemispheric syndrome is based on the directed assessment of the presence of a right arm paresis in combination with at least one of the following cortical symptoms: gaze deviation to the left, and/or aphasia, and/or erroneous performance of a complex task (earlobe-test: the fingers of the unaffected arm are required to reach to the contralateral earlobe). In the case of a right-hemispheric syndrome, the score assesses the presence of left arm paresis in combination with gaze deviation to the right, and/or neglect and or erroneous performance of the earlobe-test (without crossing the midline).[28] The test result is dichotomous

(positive when unilateral brachial paresis and congruent cortical deficits are present, otherwise negative). The identification of cortical deficits is also a central element of successfully utilised pre-hospital screening tools such as the RACE score[19] or the Vision, Aphasia, and Neglect (VAN) scale.[29]

Second, we test the score's feasibility by applying it in a simulation study, including 48 volunteers without a medical background, eight actors, and 24 medical staff (dispatchers at emergency control centres, EMS personnel, and nurses). Currently, there is little experience in using such scores during the emergency call involving LFR. We aim to achieve high sensitivity (≥0.75) and specificity (≥0.7) in the range of previously published analyses of pre-hospital stroke scales.[30] Followed by the prospective validation of the LVO score, where EMS dispatchers apply the LVO score in real-life emergency calls to screen patients with suspected stroke but still alert the usual rescue chain in parallel (N=500). The research staff assesses the validity of the LVO score.

For the implementation of the score, we develop training seminars adapted to each occupational group. The effectiveness of the EMS professionals' training is evaluated in EMS dispatchers, emergency doctors, and emergency rescue staff. Effectiveness will be tested by means of an online pre-/post-test, including case-based examples and knowledge testing, before, directly after, and three months after the training. The test comprises general questions on stroke recognition, management, treatment, as well as specific questions about the intervention itself (application of the LVO score in the field). The results allow for both descriptive and quantitative statistical analysis. In addition, all the emergency professionals involved in the rescue procedure have access to the LVO score via a mobile app, specifically created for the score assessment at the emergency site and the consolidation of knowledge by text and video explanations.

Stage 2: Consecutively, we performed a controlled study with a stepped-wedge design and clusters of six emergency control centres for gradual implementation of the intervention procedure. The intervention and control groups each include 125 patients (N=250). Enrolment began in early summer 2021. During the control phase, emergency control centres carry out emergency interrogation and dispositions in accordance with local standards. Subsequently, the six participating emergency districts move gradually from the control to the intervention phase (stepped-wedge design). Control data is available from the control phase of this design and existing retrospective datasets from patients who received MT in the Department of Neuroradiology, University Medical Centre Freiburg, between 2012 and 2020. A retrospective application of the LVO screening tool on historical cohorts is not feasible, as these examination steps are neither part of the routine clinical examination nor of frequently used stroke-screening tools, such as the National Institutes of Health Stroke Scale (NIHSS). 90 days post-stroke, a study staff member blinded to group allocation will enquire the mRS by phone from patients or their guardians (unblinded treatment and blinded endpoint evaluation).

Stage 3: A formative process evaluation assesses the intervention's feasibility. Interviews start at two time-points, during and at the end of the intervention phase, with EMS dispatchers, emergency doctors and EMS staff, air rescue staff, and LFR. The feedback from the first interview round will be used to optimise the intervention, if necessary. A workshop will be held for all the professionals involved in the study to discuss both the data and their experience with applying the procedure. This workshop aims to devise improvements for the implementation of the intervention during stage 2. We interview LFR about their level of psychological stress during the emergency call and the clarity of the EMS dispatchers' instructions. The survey conducted among EMS professionals focuses on the implementation and feasibility of the LESTOR approach, benefits and undesirable effects of the intervention.

Study setting

The study is planned for a duration of three years in South Baden, Germany, in the districts of Breisgau-Hochschwarzwald, Lörrach, Emmendingen, Waldshut, Schwarzwald-Baar, Tuttlingen and the city of Freiburg in collaboration with six emergency control centres, three air rescue services and eight hospitals.

Inclusion and exclusion criteria of participants

Eligible for inclusion are patients older than 18 years, presenting symptoms indicative of a stroke due to LVO, and meeting evidence-based inclusion criteria for treatment with MT within 24 hours of the onset of symptoms. The treatment group contains patients with suspected LVO from the six participating primary stroke centres transferred to one of the two CSCs and patients primarily treated at the respective CSC. Exclusion criteria are pre-existing severe impairment due to other diseases (according to level five of the mRS: "Severe disability. Bedridden, incontinent, requires constant nursing assistance").

Statistical analysis

Stage 1: During the validation of the new LVO score, we determine the test's performance, e.g. sensitivity, specificity and the percentage of correct classifications. Inter-observer reliability is assessed by Krippendorff's Alpha and Fleiss' Kappa. We assess the internal validation by performing cross-validation, and the external validation by comparison of the score results with vascular imaging. The knowledge gained by EMS professionals from dedicated training is evaluated in a pre-test/post-test design.

Stage 2: Ordinal logistic regressions to predict mRS will be conducted based on the following variables:

- Independent variables: group assignment (intervention vs. control)
- Confounders (control variables): e.g. age, severity of stroke (NIHSS) at onset, anamnestic data, such as atrial fibrillation, diabetes mellitus, and the location of the occlusion of the affected arteries.

We will calculate an adjusted odds ratio for a change in the mRS. Favourable clinical outcome is defined as mRS ≤2 (similar to Goyal et al.).[8] For the sensitivity analysis, we will use different cut-off values and calculate 95% confidence intervals.

We will model a cluster membership corresponding to recommendations in the literature.[31] We will perform imputation of missing values for the predictor variables, but not for the outcome variables. Missing values might occur during three different phases: First, during pre-hospital care, LVO patients might not be recognised as such in the emergency control centre and/or on site. Possible scenarios include, e.g. language barriers or atypical presentations of stroke. In these cases, the pre-hospital LVO scoring might be lacking. Second, missing data might originate during hospital care due to an early patient transfer to external hospitals after MT. As a study nurse follows up patients stringently on time, these cases will be identified quickly and missing data can be tracked. Third, information on the clinical outcome might not be obtained in cases where the systematic follow-up by our study nurse is not successful. Based on our experience during the last >10 years, we expect a high rate of complete follow-up data of >90-95%.

We will perform a complete case analysis if the proportion of missing data is below 5%. Above 5% missing data, multiple imputations with an expectation maximisation algorithm will be conducted.

A power analysis shows that testing for the statistically significant superiority of the intervention over the control group requires far more cases (N=664) than available in our target region during the study period. We therefore conduct a controlled study to explore achievable effects and practicability under routine care conditions. Due to limitations of the sample size, we will explore the clinical significance of the intervention effects and refrain from testing for the statistically significant superiority of the intervention over the control group.

Furthermore, we calculate a propensity score, which represents the probability of a patient with a particular set of initial values receiving the intervention. This enables the monitoring of group differences that may occur in a non-randomised allocation. A cost analysis will be carried out as the first part of the health economic evaluation. For this purpose, the Medical Controlling Department at the University Medical Centre Freiburg will calculate the costs incurred during an in-patient stay for both patients in the intervention and the control group. This data is available, as the University Medical Centre serves as a reference hospital in the maintenance and further development of the German Diagnosis Related Groups (G-DRG) system via the InEK Institute [Institute for Hospital Remuneration Systems].

To determine the costs of the intervention, the training costs and the averaged expenses for the additional helicopter missions are used: if the LVO score, applied by EMS dispatchers, falsely indicates a patient having LVO, the air rescue might have to return to base without a patient, resulting in additional costs. Hence, we will compare the costs of the intervention and control group.

As a final step, a cost-effectiveness analysis will be performed, whereby the primary endpoint (functional capacity, documented according to the mRS) will be expressed in relation to the total costs. Secondary endpoints are, amongst others, length of pre-hospital, in-hospital and, if applicable, inter-hospital treatment. We also asses the following:

- clinical criteria (e.g., difference between NIHSS at admission and discharge, length of hospital stay, number of hemicraniectomies and mortality)
- imaging criteria at initial imaging:
    - ASPECTS (Alberta stroke programme early CT score)
    - ischemic core volume (ml)
    - perfusion-lesion volume (ml)
    - mismatch (core/penumbra)
    - early signs of ischemia
    - occlusion side
    - extra- and intracranial location of the occluded segment
    - TICI (thrombolysis in cerebral infarction) score
    - bleeding type, side, diameter (mm), and location

- imaging criteria at follow-up:
    - time and frequency of ischemia or intracerebral haemorrhage, or their combination
    - infarct volume
    - bleeding volume

As logistics in stroke care is complex, we will systematically record time metrics regarding both the pre-hospital (e.g., emergency call to hospital admission), and intra-hospital processes (e.g., door to recanalisation). This might streamline the management of LVO stroke patients.

Stage 3: Trained interviewers conduct guided, semi-structured telephone interviews. The interviews allow a broad exploration of diverse aspects of a phenomenon when there are few theoretical and empirical findings within a particular research field, as in the present study.[32] Interview questions deal with the implementation of the intervention, its barriers, any unfavourable side effects, problems, and solutions. The interviews are recorded on tape and transcribed. The qualitative content analysis is performed according to Mayring.[33]

Discussion

The high mortality and morbidity rates associated with stroke highlight the importance of this study. The LESTOR study aims to promote the ultra-early identification of patients with LVO by addressing the pre-hospital triage phase and optimising the stroke rescue chain. The involvement of LFR along with the administration of a dedicated LVO score during the emergency call may be crucial in accelerating the time to treatment for stroke patients with LVO, thereby improving the clinical outcome.

Effect size determination will allow for a preliminary assessment of effectiveness and facilitate power considerations for larger studies with a higher sample size. However, the hypothesis of a statistically significant difference between the intervention and control groups cannot be tested because of the limited sample size.

We do not expect any disadvantages for patients when applying the score by the EMS dispatchers since the ambulance is on its way when the score assessment begins. If the score assessment fails and LVO-positive cases are missed, e.g. due to technical problems or language barriers, patients receive standard care, which might well prove to be disadvantageous compared to the intervention. The detailed assessment of advantages or disadvantages by data and process evaluation is a central purpose of our study.

The results addressing the ultra-early identification of patients with LVO will be disseminated to the public via conferences and journal publications.

Conclusions

To the best of our knowledge, this is one of the first studies that apply a pre-hospital score to identify LVO in collaboration with LFR during an emergency call and evaluates the implementation, feasibility and costs of this intervention.

If the implementation of the dedicated LVO score demonstrates positive effects on the pre-hospital identification of LVO, duration of the rescue, and health outcomes, it should be assessed for its application potential in the long-term in other regions. The results and effect sizes detected in our study will provide an important basis for future studies with larger sample sizes. The process evaluation will provide additional insight into how the participating emergency professionals perceive the intervention and the psychological impact on LFR.

Abbreviations

ASPECTS
Alberta stroke programme early CT score
CPSS
Cincinnati Pre-Hospital Stroke Scale
CSC
Comprehensive stroke centre
EMS
Emergency medical service
EMSA
Emergency Medical Stroke Assessment

FAST
Face-Arms-Speech-Time
G-DRG
German Diagnosis Related Groups
LFR
Lay first responder
LVO
Large vessel occlusion
mPASS
modified Prehospital Acute Stroke Severity Scale
mRS
modified Rankin Scale
MT
Mechanical thrombectomy
NIHSS
National Institutes of Health Stroke Scale
PASS
Prehospital Acute Stroke Severity
SSTS
Stockholm Stroke Triage System
RACE
Rapid Arterial oCclusion Evaluation
TICI
thrombolysis in cerebral infarction
VAN
Vision, Aphasia, and Neglect

Declarations

Monitoring

A DMC is not needed as known risks are minimal and study focus is on feasibility and costs of the intervention.

Sponsoring

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Ethics approval and consent to participate

Ethical approval for this study was obtained from Ethics Committee at University of Freiburg (Reference number 416/20; 08.10.2020). All procedures were performed in accordance both with the ethical standards of the institutional or national research committee, and the 1964 Helsinki Declaration and its later amendments or with comparable ethical standards. This study protocol adheres to the recommended SPIRIT Checklist.

Consent for publication

Written informed consent will be obtained from all subjects from the pilot phase, the online pre-/post-test and the interviews.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DR, NZ and FS wrote the manuscript with support from AN, EFG, JB, SM, MLH and UB. EFG, FS und JB conceived and designed the study and supervised the project. All authors contributed to refinement of the study protocol and approved the final manuscript.

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