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E-66

Decision Making in The Emergency Medicine

# Possibilities for reducing prehospital delay in acute ischemic cerebrovascular events

Doctoral (Ph.D) thesis

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## Introduction

Cerebrovascular diseases constitute a group of major importance for public health today. Although in Hungary in the 21st century most deaths are caused by cancers and diseases of the circulatory system, stroke is now the third most common cause of death, since on average over the past 10 years 12,300 deaths per year have been due to cerebrovascular disease (KSH [Hungarian Central Statistical Office], 2021). Around the globe, approximately 26 million people suffer from stroke every year, making it the second leading cause of death worldwide and the leading cause of disability, thus it has a significant impact on quality of life (Kamel et al, 2017). This demonstrates that stroke is one of the most urgent medical conditions of our time, and it includes all sudden onset focal and less frequently global neurological syndromes that persist for more than 24 hours or cause death within 24 hours and have no demonstrable cause other than a change in cerebral circulation (Truelsen et al, 2000).

In acute stroke, early diagnosis of the disease and accurate determination of the onset and detection of symptoms are essential for the restoration of cerebral function (impairment of cerebral function is initially reversible) or at least for the reduction of the degree of impairment. The first few hours after the onset of stroke are essential in determining the further fate of the patient. This is one of the reasons why the concept of the "golden hour" should be emphasised. The most important aim is to minimize the time between the onset of the first symptoms and initiation of definitive care (Ruiz et al, 2018) (Gonzalez et al, 2019).

Although the relationship between the elapsed time and the course of stroke is not linear, the importance of the time factor in the course dynamic of stroke is unquestionable. Over time, the deterioration of the stroke patient's condition (the progression of the disease) gradually slows down, that is the importance of time decreases continuously, primarily due to the intensity of the collateral circulation and the quality of the blood flow of the penumbra, although significant individual variations can be detected. An important consequence is that the therapeutic time window also shows significant variability with elapsed time, different clinical conditions, and the availability of penumbra-perfusion. This finding draws attention to the fact that due to the variability of the time window, and irrespective of the duration of stroke, it is necessary to shorten the time to definitive care, i.e. the pre-hospital delay, while also maintaining the penumbra's circulation (Gomez et al, 2018). Usually the ambulance service is the first link of care and therefore in charge of the essential elements of pre-hospital care which include determination of the diagnosis, stabilising the patient's condition, recognising and treating reversible causes and complications, as well as determining whether definitive therapy is available, starting definitive therapy if possible, and taking account of potential risks.

**Objectives**

The primary goal of organising the patient pathway in case of an acute stroke is time management, that is to minimise time loss given that every single minute of delay in obtaining definitive care after the onset of the first symptoms means that the patient's healthy life years will be reduced by an average of 1.8 days (Meretoja et al, 2014). According to the AHA/ASA recommendations of 2018, the "door to needle time", i.e. the time from delivery of the patient to the hospital to the start of definitive therapy should not exceed 60 minutes. The therapeutic time window is narrow, but this time frame may vary individually according to a number of factors. It is therefore crucial to reduce pre-hospital delay by seeking to minimise the duration of pre-hospital care provided at the scene. The "load and go" principle can be designated as one of the means of achieving the stated goal, which means transporting the patient to a care facility after administering minimal care. Another option is to use the transport time itself to shift the administration of definitive therapy forward in time. Accordingly, the time between arrival at the scene and arrival at the stroke centre ("field to door time") is included in the "door to needle" time by the pre-hospital care provider by reducing the care to a minimum that is sufficient to allow definitive care. This requires that the pre-hospital care provider recognizes the disease process as stroke, and is able to prepare the patient for definitive therapy, the conditions of which must necessarily be available to them. The aim should always be to accurately determine the time of onset and/or detection of stroke symptoms, and as a result, collecting relevant information about the connection between the disease and the therapeutic time window. Recognising the fact that stroke treatment is limited by the time window, it is necessary to weigh what therapy is needed and what interventions are necessary. In cases where the intervention is not necessary, clearly the "load and go" approach shall be applied. In cases where the preparation of the patient for intervention may be necessary to perform the definitive therapy in time, pre-hospital care is important, and can possibly be performed using the transport time.

Overall, because of the time-dependent nature of stroke, even a minimal delay after the onset of the disease process can significantly reduce a patient's life expectancy. In this context, our research aimed to explore a broad spectrum of factors that are already present on the lay side as factors affecting the waiting time and on the pre-hospital care providers' side as factors that result in unjustified additional time in the pre-hospital phase of the stroke patient pathway.

**Samples and methods**

We conducted our research in three phases in order to map the time intervals taken during (the different stages of) the stroke patient pathway in order to identify the reasons for delays and to draw clear conclusions upon which to base recommendations for time saving.

***First research phase, Sample "A" (N=202)***: The target group was lay people with no medical/health education who had suffered a stroke ("Sample A"). A self-administered questionnaire survey was conducted in this group. The research was a descriptive, prospective, qualitative study conducted between 01 February 2017 and 31 August 2017. According to the methodology, the survey covered socio-demographic data such as the gender, age, highest level of education and type of residence of the

respondent. The questions also included past and present chronic illnesses, the person who noticed the stroke symptoms, what symptoms were noticed, the first provider called for help after the stroke was noticed, and the time of the first call for help. The study focused on two main factors: the length of hesitation time and stroke knowledge, the latter of which included the time-dependent nature of the disease process, knowledge of risk factors, lay score systems and conditions that mimic stroke.

***Second research phase, Sample "B" (N=220)***: The research was a quantitative, cross-sectional, retrospective study, which analysed the case documentation forms of presumed stroke patients treated and transported to hospital by the Somogy County units of the South Transdanubian Region (DDR) of National Ambulance Service (OMSZ) between 01.01.2017 and 31.12.2017. During data collection, we selected case documentation files with the referral diagnosis of stroke, acute ischaemic stroke, transient ischaemic attack (TIA), cerebral events, cerebral apoplexy, cerebral haemorrhage, and ICD codes: I60–I69 (276 cases in total). Next, documentation files of patients with recurrent or resolving stroke, tonic and/or clonic seizures with unconsciousness, and cases where we failed to obtain relevant data due to lack of documentation were excluded from the study.

***Second research phase, Sample "C" (N=264)***: We conducted a descriptive, prospective, quantitative study, analysing the stroke patient pathway in two stages. First, we recorded the information provided by the case documentation forms generated during pre-hospital care, for which the data collection was conducted at Ambulance Station 1 in Pécs, Baranya County of the South Transdanubian Region of OMSZ between 1 January 2017 and 31 December 2017. Subsequently, in the second stage, the follow-up of the patients was performed at the Emergency Department (SOB) of the Faculty of Emergency Medicine (SOT) of the University of Pécs Clinical Centre (PTE KK). Our target group for the study included all patients admitted to the Emergency Department of the PTE KK by the OMSZ whose case documentation forms showed one of the following referral diagnoses: stroke, ischaemic stroke, acute stroke, TIA, cerebral event, haemorrhagic stroke, cerebral apoplexy. The data collection covered the full data set using convenience sampling. Patients who had a target-matched referral diagnosis in their case documentation forms filled out by the OMSZ were selected for participation in this phase of our study (N=292). We excluded those who were under 18 years of age, or had incomplete or illegible pre-hospital case documentation or hospital documentation.

***Second research phase, Sample "D" (N=280):*** For our retrospective cross-sectional, quantitative research, data collection was carried out in two intervals. In the first phase, we analysed the final hospital discharge reports of patients who were admitted by ambulance to the Emergency Department of the PTE KK SOT between 01 January 2018 and 31 October 2018 and had a definitive diagnosis corresponding to the target group. In a second phase, the pre-hospital case documentation forms of these patients were retrieved and their data were analysed. Our target group for the study included all patients admitted to the Emergency Department of the PTE KK SOT by the OMSZ whose discharge reports showed one of the following diagnoses: stroke, ischaemic stroke, acute stroke, TIA, cerebral event, cerebral apoplexy, ICD codes: I63–I69. The data collection covered the full data set using convenience sampling.

Patients (N=338) who had an intra-hospital diagnosis matching the target group and were admitted by ambulance were included in the sample for this phase of the study. Subsequently excluded were those who were under 18 years of age, or had incomplete or illegible pre-hospital case documentation or hospital documentation, whose stroke was improving, or were transferred by secondary transport to a definitive care site.

***Third research phase, Sample "B" (N=220):*** In our third research phase, we examined the interventions carried out by the ambulance units and their justification, based on the "B" sample of the second research phase. For our cross-sectional quantitative study, data collection was carried out at two stations of the National Ambulance Service in Hungary in two cities with a population of approximately 65,000, with a coverage area of 15 to 20 municipalities per station. The levels (BLS and ALS) of the two ambulance service stations and their service hours were the same. In the study, we analysed case documentation files of patients with a preliminary diagnosis of ischaemic stroke, as determined by the ambulance service units, who received care and were transported to hospital by the ambulance service units between 1 January 2018 and 31 December 2018. Patient identification data were not recorded, and patients were kept anonymous throughout the study. During data collection, we selected case documentation files with the referral diagnosis of stroke, acute ischaemic stroke, transient ischaemic attack (TIA), cerebral events, cerebral apoplexy, cerebral haemorrhage, and ICD codes: I60–I69 (276 cases in total).

Next, documentation files of patients with recurrent or resolving stroke, tonic and/or clonic seizures with unconsciousness, and cases where we failed to obtain relevant data due to lack of documentation (56 patients in total) were excluded from the study.

Data from the four samples of the three phases of our research were analysed using SPSS version 26.0 statistical software. Descriptive statistics, chi-square test, two-sample t-test, Mann–Whitney test, correlation calculation, and variance analysis were used. Significance level was determined to be $p<0.05$ with 95% confidence interval (CI: 95%).

## Results

### Testing our Hypothesis 1

*The results of our study of sample **"A"** confirmed our hypothesis **H1** that the knowledge rate of stroke symptoms and their severity is independent of the knowledge of the scoring systems that help to detect them.*

In the first phase of the research, we focused on the period when detection by a lay person is the first link in the stroke survival chain. When examining the entire stroke patient pathway, the "onset to needle" time can be divided into pre-hospital and in-hospital delays. In this phase of the research, we investigated the hesitation time, which is of paramount importance for the pre-hospital delay, and which is manifested in the lay person's delay in seeking help. The earliest possible recognition of stroke symptoms and immediately calling for ambulance are crucial factors in the patient's life expectancy.

In summary, the responsibility of the lay person in the outcome of stroke is not negligible, as the increase in the hesitation time is accompanied by an increase of neuronal death, a major determinant of patient survival.

In order to explore the causes of the factors leading to an increase in hesitation time, we selected the lay stroke survivors of the first phase as our sample. With regard to the underlying chronic diseases that are primarily responsible for the development of stroke, hypertension (69.3%) was the dominant condition in our sample, in line with data published in the international literature, with the additional risk factors of diabetes mellitus (17.3%), high cholesterol level (12.9%) and atrial fibrillation (14.4%) co-morbidities also present, but in a smaller proportions. In terms of specific stroke symptoms, patients or their relatives most frequently experienced/detected aphasia (39.1%) and facial paresis (39.1%), and paresis/hemiparesis (37.6%) and hemiplegia (37.1%) in smaller proportions. An important issue is whether the patient perceives the onset of symptoms on their own or they are detected by those around them, as this can have a major impact on hesitation time.

In our sample, in 64.4% of the cases people in the patients' environment detected the onset of symptoms, which raises the possibility that if the patient was alone at the onset of the stroke, this may have had a greater influence on the increase in hesitation time, i.e. the call for help was made later. Our results refute this, as there was no measurable association between the increase in hesitation time and the identity of the person who experienced/detected the stroke symptoms ($p=0.244$).

The results show that in the case of the majority (78.2%) of patients the call for ambulance was made within the 3 to 4.5-hour therapeutic window used at the time of the study, although it is not insignificant that hesitation time could have been further reduced if an ambulance call had been made immediately after the onset of symptoms. Indeed, the results showed that less than half of the patients in the sample called the ambulance service immediately after the onset of stroke (48%), and they most often reported the onset of symptoms to a relative or their GP.

The international literature on this topic suggests that the severity of the stroke, i.e. the concurrent presence of specific stroke symptoms, plays a role in defining hesitation time. We found that, in isolation, hemiplegia among the specific symptoms was the trigger for the primary ambulance call ($p=0.04$), but there was no measurable difference in the time from symptom onset to ambulance call compared to other specific stroke symptoms. If aphasia was detected in the patient, it did not affect the time to the primary ambulance call ($p=0.450$), but did affect i.e. reduced the hesitation time ($p=0.048$). We hypothesised that the concurrent presence of several specific symptoms would have a positive effect on the time to the primary call for ambulance and also on hesitation time. We found that a suspected major stroke only affected the immediate call for ambulance ($p=0.05$), while it did not affect hesitation time ($p=0.944$).

Based on these results it appears that the isolated or concurrent occurrence of different specific stroke symptoms affected either the time of the primary ambulance call or the reduction in hesitation time, but not both together. However, among patients in the sample with a history of a previous stroke, we found that they called the primary call for ambulance (p=0.041) and did so within 30 minutes (p=0.037), therefore the previous stroke had an effect on reducing the hesitation time.

Among lay people, knowledge of the FAST scoring system for stroke detection would be expected to help reduce hesitation time. Only 25.7% of our sample had previous knowledge of the scoring system. However, our results clearly show that among patients who were aware of the FAST score, this knowledge had no effect on the primary ambulance call (p=0.132) or on the reduction of hesitation time (p=0.327).

In conclusion, this part of our study suggests that among lay patients the factor reducing the primary delay is an increase in the recognition rate of stroke symptoms, rather than the dissemination of scoring systems promoting the recognition.

***Testing our Hypothesis 2***

*The results of the study of sample **"B"** of this research phase supported our assumption that there is a difference in the time spent at the scene by different level units (EK [High level emergency case vehicle] / ROKO-ALS [Advanced level emergency vehicle], MGK-BLS [Basic level emergency vehicle]). It is therefore the responsibility of the rescue management to alert an ALS unit only in case of a need for a higher level intervention, as this can significantly reduce pre-hospital delay.*

One of the focal points of the second phase of our research was the length and usefulness of time spent on site, and we also examined which factors influence these measures and how they could be changed. The results of our study show that pre-hospital time intervals show significant differences. It is mainly the responsibility of the patient and the pre-hospital care provider to remain within the therapeutic time window, so it must be judged and ensured accordingly.

Based on this, the first step in our study was to analyse how care is affected depending on whether the stroke patient receiving care is within the therapeutic time window. Examining the time to arrival at the scene, we found that it was independent of the stroke time window (p=0.626) and the level of the ambulance unit (p=0.663).

Since during the research we were unable to obtain information on the factors influencing the time of departure from the rescue centre and arrival of the ambulance at the scene, it can be concluded that the ambulance tried to arrive at the scene as soon as possible, regardless of whether it was clarified to the personnel at the time of notification that the stroke case was or was not within the therapeutic window.

Our data show that on-site time spent during pre-hospital care is higher for ALS-level ambulance units (20.08 minutes) than for BLS level ambulance units (13.95 minutes).

The possible reasons behind our observation: It is possible that the ALS level units may delay patient examination due to the availability of a physician and the presence of advanced devices. Under current protocols, if the risk of stroke is even minimal according to mCPSS, the patient should be transported to the nearest institute that provides definitive care as soon as possible because stroke is time-sensitive and has a high time factor, and this possibility cannot be the reason for the delay, especially in the case of patients within the time window, although based on our results, this fact does not reduce delay either ($p=0.420$). Another possible explanation for the increase in on-site time may be the delay in deciding on the patient pathway, but this cannot be accepted either because protocols currently in force clearly define and regulate patient pathways. From our sample, we excluded cases where a higher level of intervention would have been required, thus such cases could not have extended the time spent at the scene. All this suggests that the longer time spent on site by ALS level units may be explained by unwarranted instrumented or instrumentless patient testing (e.g. unwarranted 12-lead ECGs, neurological testing beyond the elements of mCPSS) or therapy at the scene, which may be shortened by the emergency care provider's awareness that in the case of a patient with a suspected stable stroke the level of care is identical to that provided by BLS competent units.

In order to reasonably reduce pre-hospital delay, we examined which factors influence it. The ABCDE rapid status assessment clearly identifies for the pre-hospital care provider what additional tests are needed to establish a particular referral diagnosis and how to intervene to slow down the course dynamic of the disease and stabilise vital signs.

Even in the case of only one positive symptom on the mCPSS, the caregiver should consider the diagnosis of stroke and care accordingly for the patient, and further aim to provide definitive care as quickly as possible while protecting the penumbra and the collateral circulation.

This is not consistent with our finding that in stroke patients with aphasia, ALS level units spent more time at the scene than in the case of patients with no speech disorder ($p=0.038$). When looking for causes, we should exclude the possibility that treating a patient with aphasia would be a more complex challenge for the pre-hospital care provider, as it does not differ from the treatment of patients with other stroke symptoms, especially at the level of an ALS ambulance unit. The only reason we can identify for the delay is the self-serving requirement to determine the diagnosis of speech disorder and to determine its type, and not the fact that additional examinations or interventions are required. In conclusion, this delay can be reduced by providing advanced trainings to healthcare providers making them of the fact that motor or sensory aphasia has no effect on therapy, it is merely a symptom that increases the likelihood of the diagnosis of stroke, and therefore detecting this symptom should in no way prolong the duration of pre-hospital care.

When examining the time spent at the scene, we found that the following factors require additional consideration: measuring blood glucose levels with a device significantly prolongs the duration of care compared to cases when blood glucose levels were not measured, but only in the case of BLS level ambulance units ($p<0.001$).

Our hypothesis that the cause of this is to perform indicated interventions to resolve pathological blood glucose level is not borne out by our findings. In fact, it was clearly demonstrated that there was no significant difference between the duration of care at the scene and the subsample where the patient experienced hypo/hyperglycaemia (p=0.836).

The transport time, that is the time required to transport the patient from the scene to the definitive point of care, was not affected by the level of ambulance unit (p=0.685) or the time window (p=0.507). Our analyses of the duration of transport did not address the question of what determines transport time. In our opinion, at this stage of the stroke patient's pathway, if the time cannot be influenced, at least the quality of transport to the hospital should be changed given the trauma of transportation.

***Testing our Hypothesis 3***

*The results of our study of sample **"C"** disproved our hypothesis **H3** that in the case of patients with suspected stroke within the therapeutic time window a shorter pre-hospital delay can be sustained, since the time window had no effect on the time from arrival at the scene to arrival at the hospital.*

***Testing our Hypothesis 4***

*The results of our study in sample **"C"** confirmed our hypothesis **H4*** that *while the pre-hospital care providers' stroke guidelines are adequate, there are differences between the different levels of the ambulance units.*

Coordination between different levels of care systems is essential to maximise the patient's life expectancy. In this phase of our research, we have therefore sought to investigate the times spent in the pre- and intra-hospital phases and to identify any factors that might influence them. Regarding the time between arrival at the scene and hospitalisation, similar to what was observed in our sample **"B"**, the pre-hospital phase of care was not influenced by whether or not the patient was within the therapeutic window. In fact, our results clearly show that there was no significant reduction in time either globally (p=0.914) or in sample subgroups divided according to ALS (p=0.360) or BLS (p=0.360) ambulance units.

There are two possible causes behind these results: It may be assumed that pre-hospital care providers do not put enough emphasis on the recording of the anamnesis, thus not clarifying the exact time when the complaint was detected and thus not clarifying whether the patient is within or outside the therapeutic time window. Other data suggest that even if the care providers identify that the patient is within the time window, they do not apply the "load and go" approach. At the same time, the procedures in force clearly specify that the exact timing of the onset of the complaint must be recorded in the event of a stroke, and the issue of a time window also arises in the case of the notification of a preliminary definitive care provider defined in the protocol.

Accordingly, in case of a suspected stroke the only acceptable possible reason would be for pre-hospital care providers to try to get the patient to the definitive point of care as soon as possible, regardless of whether the course of the stroke is within or outside the therapeutic time window.

However, the above mentioned plausible reason is contradicted by our results which highlighted that in cases where the ongoing stroke was confirmed during the intra-hospital care, the mean pre-hospital delay was reduced by 4.41 minutes on average (p=0.004). This suggests that the severity of stroke symptoms, rather than being within the time window, may be the primary factor influencing the time from arrival at the scene to arrival at the hospital.

However, when examining the intra-hospital phase, it can concluded that in cases where the patient was treated within the time window, there was a significant reduction in the "door to CT" time compared to cases outside the time window (p=0.015). This suggests that stroke patient pathways could be reduced if, in addition to the time gained in the in-hospital phase, the pre-hospital phase was also more affected by need to remain within the time window. However, the 3–4.5-hour time window for the pre-hospital phase in force at the time of the study has been replaced by a 24-hour time window, which reduces the negative implication of the above results, but not the effect on neuronal death.

Regarding the intra-hospital confirmation of stroke referral diagnosis given by different levels of ambulance units, the rate of hospital-confirmed stroke cases transported by BLS units was higher than that of ALS units (p=0.048). This shows that although the pre-hospital care providers' stroke referral diagnosis is adequate in our sample, differences can be observed between the different levels of the ambulance units. Consequently, due to the time-sensitive nature of stroke, the pre-hospital care provider should ensure that the proportion of false-negative cases is minimised, even at the cost of increasing the proportion of false-positive cases.

On the positive side, we conclude that where an intra-hospital CT confirmed the presence of stroke, the length of the patient pathway was more than 2 hours shorter compared to cases where no stroke was confirmed (p<0.001). If we consider cases within the time window, the length of the stroke patient pathway is even further reduced compared to cases outside the time window (p=0.002).

***Testing our Hypothesis 5***

*The results of our study of sample **"D"** highlighted the primary point of our hypothesis **H5**, that the quality of the application of scoring systems is worse in the case of lower level ambulance units. Our hypothesis that the referral diagnosis posited by the MICS at the time of notification has an impact on the referral diagnosis given by the ambulance unit at the scene was confirmed specifically for the BLS units.*

One of the specificities of pre-hospital care is that the availability of instrumented tests beyond simple, instrument-free tests is limited at the patient's location. Due to this fact, a relevant assessment of the patient's complaints and symptoms, as well as an accurate understanding of the patient's history is crucial in the detection of high time-factor/time-dependent pathological processes. The limited diagnostic value of the available tests makes the use of different scoring systems especially important for establishing a referral diagnosis at the scene.

Consequently, in sample **"D"** of our second research phase, we investigated the effectiveness of the use of the mCPSS system, which assumes an ongoing stroke, among on the scene care providers and the influence of the pathological process assumed by MICS on the formulation of the referral diagnosis.

In order to test with certainty our hypothesis described above, only cases with a definitive intra-hospital diagnosis of stroke were included in the sample. In care provided by an ambulance unit, which is a pre-hospital speciality, if a single symptom is positive according to the mCPSS, there is a 78% chance of an ongoing stroke, which suggests that taking into account the time dependence, the pre-hospital care provider must adhere to a "load and" go approach. When looking at the presence of aphasia component of the scoring system, significance ($p<0.001$) was detected at the BLS level of the ambulance units, i.e. aphasia was more often deemed to be present during pre-hospital care than recorded during intra-hospital care. The underlying reason for this may be, on the one hand, the incorrect performance of aphasia testing. However, this reason can be dismissed in light of the fact that the ambulance service places great emphasis on annual continuing education, which includes the examination of stroke patients. The only acceptable reason is an improvement of the stroke, i.e. a moderation of symptoms measured in the pre-hospital phase compared to the symptoms measured in the intra-hospital phase. We seemed to detect a similar factor in our results indicative of central facial palsy. Indeed, statistical tests highlighted that, compared to the central facial paresis experienced in intra-hospital care, both BLS ($p<0.001$) and ALS ($p=0.011$) units more frequently marked it as presenting symptom during pre-hospital care. We must reject the hypothesis that rescue care providers may have also evaluated peripheral facial paresis as a stroke symptom, because only patients with a definitive diagnosis of stroke were included in our sample **"D"**. We can therefore also identify improving stroke as the only cause. On the positive side, the fact that aphasia and central facial paresis were more frequently reported by the on the scene providers compared to the intra-hospital ones suggests that more emphasis is being placed on the assessment of these elements of the mCPSS, which forms the basis for determining the referral diagnosis.

We then compared the on the scene identification rates for upper and lower limb paresis and plegia, and for paresis/hemiparesis and hemiplegia affecting one half of the body measured in the mCPSS with those measured at the definitive care site. The results showed that, except for any lower limb paresis, BLS units had a worse identification rate compared to ALS units for upper limb paresis ($p=0.001$), upper limb plegia ($p=0.002$), paresis/hemiparesis ($p=0.015$), hemiplegia ($p=0.006$) and lower limb paresis ($p=0.029$) compared to those measured during the intra-hospital phase. We hypothesise that the following factors may be involved in this difference. It is possible that lower level ambulance units place more emphasis on the examination of aphasia and central facial paresis, and in case of their positive identification, omit the examination of the limbs. However, our results clearly refute this, as it was shown that if the BLS units at the scene found a lower or upper limb plegia or hemiplegia in addition to the aphasia and central facial paresis, the patient was also given a referral diagnosis of stroke ($p<0.001$).

Another reason could be the problem of distinguishing paresis from plegia, i.e. the care providers do not consider weakened muscle strength as a positive symptom, but only a completely paralysed limb or body part. This rationale is supported by our finding that there was no significant difference between the stroke referral diagnosis and upper/lower limb or paresis/paresis in the intra-hospital setting ($p=0.746$).

In addition to the effective use of mCPSS, the influence of the referral diagnosis provided by MICS on the on the scene diagnosis is a key issue. We hypothesised that there was some degree of influence on pre-hospital care providers, which was confirmed by statistical tests ($p<0.001$). The results showed that at the level of ambulance units, there was no effect of preliminary diagnosis on the diagnosis formed by ALS units, as all cases they attended were assumed to be stroke (n=55), whereas a relationship was detected in the case of lower level BLS units ($p<0.001$). As a positive result, BLS units did not receive a stroke preliminary diagnosis in 17.10% (n=38) of their own cases, but did give a stroke referral diagnosis to their patients, although we believe that this proportion could be increased with the use of a more effective patient screening and scoring system. The overly large influence of the MICS preliminary diagnosis based on anamnesis information at the BLS unit level is suggested by our finding that in 18 cases stroke was neither an MICS referral diagnosis nor a referral diagnosis by the ambulance unit.

In our opinion, the variables examined in our sample point to the possibility that some degree of improvement may be possible in false-negative cases where no stroke referral diagnosis was recorded. Our results provide clear evidence that the above-mentioned problem areas are significant issues for lower level BLS units. In conclusion, the time-sensitive nature of stroke requires the development of rapid diagnostic skills of pre-hospital care providers, which can be effectively achieved by the skilful use of scoring systems and the reduction of the overly influencing effect of patient history.

Awareness of this is essential especially since the other samples show that the majority of stroke cases are seen by BLS-level units, and therefore these units have paramount responsibility in making a stroke referral diagnosis and planning an appropriate patient pathway.

***Testing our Hypothesis 6***

*In the third research phase, the results of our study on sample **"B"** supported our hypothesis that there was a measurable difference between the level of ambulance units and the correctness of the decision on justified/unjustified therapy, which also has an impact on pre-hospital delay.*

During patient care, the ambulance unit is expected to initiate on-site time-increasing therapy when it is indicated and in cases where this is not warranted they should avoid such therapy and promote definitive therapy by rapid transport. As a result, the ALS level units made the right decision in 59.62% of the cases, while the same was true for 80.36% in the case of BLS units. If intervention is required, ALS units perform it correctly at higher rates (79.17%) than BLS units (62.50%).

Accordingly, in cases where the person dispatching emergency medical care considers the use of pre-hospital therapy indicated, alerting an ALS unit may be rational, but this can only be achieved by increasing the duration of care performed at the scene.

It also argues against the routine alerting of ALS units that indicated interventions were not performed in a significant proportion of cases (9.62% of the cases, while this proportion was only 3.57% in the case of the BLS units).

The analysis of the proportion of stroke patients not requiring intervention (42.86% for ALS units and 82.24% for BLS units) made it clear that in stroke patients not requiring care based on the preliminary evaluation, a BLS unit should be alerted. Thus, the time gain for definitive therapy can be maximised.

Less favourable proportions for highly trained units may be due to the fact that BLS-level units follow protocols and procedures more closely, whereas ALS units tend to make individual decisions.

It can be concluded that, in the absence of acceptable indication, on-site delays, especially for advanced level (ALS) units, must be dealt with deliberately, even after the emergency report, and the person organising emergency pre-hospital medical care should make the decision accordingly.

Because the on-site delay of ALS units often involves not indicated interventions, we cautiously advance the claim that the patient gains more time and consequently retains more healthy brain tissue if a BLS unit is sent to the scene.

The only exceptions are when, based on the emergency call, it can be concluded that an ALS unit equipped with a physician will be required (unconscious patient requiring advanced intervention) and when it would take longer for a BLS unit to reach the scene, which can be further delayed by the need for a physician-staffed ambulance unit. Our samples demonstrate that the ALS units spent over 4 more minutes at the scene, the total pre-hospital period, that is the "field-to-needle" time can be reduced with this time by alerting a BLS unit, as long as the time to the arrival of the BLS unit at the scene is no more than 4 minutes longer compared to that of the ALS unit.

In our subsample where the ALS unit provided care for a patient by performing a non-advanced intervention that the BLS unit could have performed adequately as well (at that time the average duration of pre-hospital care was: 45.65 minutes), the duration of care exceeded the duration of care in cases where BLS units could have performed the intervention (average duration of pre-hospital care was 43.04 minutes).

From the point of view of reducing pre-hospital delay, a result we should consider is that when a BLS unit is alerted, the average duration of pre-hospital care is lower even in cases when indicated or not indicated interventions are performed (43.04 minutes) compared to cases when a ALS unit is alerted, and no intervention is performed (43.22 minutes). However, definitive therapy can be initiated at the earliest if a BLS level unit is alerted to the scene and the patient's condition allows the unit not to perform any intervention. In this optimal situation, the pre-hospital delay is reduced to 38.99 minutes.

Further research may be performed to determine whether the optimal 38.99 minutes achieved by the BLS unit can be further reduced by earlier detection of aphasia and by performing blood glucose measurement during the transport period.

**New scientific results**

- Knowledge of stroke symptoms and their severity is independent of knowledge of the examined scoring system aiding stroke detection. Hesitation time was reduced by severe stroke symptoms and repeat stroke.
- For patients with suspected stroke within the therapeutic time window, the time window had no effect on the time from arrival at the scene to transport to hospital, and it only influenced the intra-hospital stroke patient pathway.
- The time spent at the scene by different levels of ambulance units (ALS, BLS unit) is different, and pre-hospital delay can be reduced by alerting the appropriate level of unit to the scene.

- Stroke referral diagnosis for pre-hospital care is adequate, but there are differences between different levels of ambulance units.
- The quality of the application of the scoring systems is worse for lower level ambulance units, and the referral diagnosis assumed by the MICS at the time of reporting influences the referral diagnosis given by the unit.
- Measurable differences can be observed between the level of the ambulance units and the correctness of the decision on justified/unjustified therapy.

**Recommendations**

- Among lay patients the factor reducing the primary delay is an increase in the recognition rate of stroke symptoms, rather than the dissemination of scoring systems promoting the recognition.
- To reduce the time spent on the scene:
- When a single positive symptom in the mCPSS is detected, the provider should assume an ongoing stroke; performing other neurological examinations outside the mCPSS elements is unwarranted.
- In the case of aphasia, it is necessary to establish the fact of aphasia; performing additional investigations to identify its type may increase the delay.
- The performance of an instrumented blood glucose measurement is mandatory but must not add meaningfully to the time spent on the scene.
- Establishing peripheral venous access can only allowed to increase the time spent on site if it is justified. 12-lead ECG/TTECG can only allowed to increase the time spent on the scene if it is justified.

- Stroke patient pathways could be reduced if, in addition to the time gained in the in-hospital phase, the pre-hospital phase was also more affected by the need to remain within the time window. *(The 3–4.5 hour time window for the pre-hospital phase in force at the time of the study has been replaced by a 24 hour time window, reducing the negative implications of our results above, but not the impact on neuronal death.)*
- The development of rapid diagnostic skills of pre-hospital care providers is necessary, which can be effectively achieved by the skilful use of scoring systems and the reduction of the overly influencing effect of patient history.
- A significantly higher proportion of BLS units made the correct decision within their own cases. Based on these findings, it is suggested that there is a need to train ALS units to follow the stroke care protocol more accurately, thereby eliminating the need to initiate unwarranted interventions that take time at the scene.

- It is recommended that from the rescue organisation side, ALS units should only be alerted when it can be concluded from the notification that a higher level of intervention will be required or BLS units can only arrive on the scene with a longer alert time. However, in cases that do not require intervention on the basis of a report it is recommended that BLS level units are alerted, as even if they intervene unnecessarily, the time spent on the scene is shorter than in cases of ALS units that do not initiate therapy at all.

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