Reasons for Prehospital Delay in Acute Ischemic Stroke

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Background—Prehospital delay reduces the proportion of patients with stroke treated with recanalization therapies. We aimed to identify novel and modifiable risk factors for prehospital delay.

Methods and Results—We included patients with an ischemic stroke confirmed by diffusion-weighted magnetic resonance imaging, symptom onset within 24 hours and hospitalized in the Stroke Center of the University Hospital Basel, Switzerland. Trained study nurses interviewed patients and proxies along a standardized questionnaire. Prehospital delay was defined as >4.5 hours between stroke onset—or time point of wake-up—and admission. Overall, 336 patients were enrolled. Prehospital delay was observed in 140 patients (42%). The first healthcare professionals to be alarmed were family doctors for 29% of patients (97/336), and a quarter of these patients had a baseline National Institute of Health Stroke Scale score of 4 or higher. The main modifiable risk factor for prehospital delay was a face-to-face visit to the family doctor (adjusted odds ratio, 4.19; 95% CI, 1.85–9.46). Despite transport by emergency medical services being associated with less prehospital delay (adjusted odds ratio, 0.41; 95% CI, 0.24–0.71), a minority of patients (39%) who first called their family doctor were transported by emergency medical services to the hospital. The second risk factor was lack of awareness of stroke symptoms (adjusted odds ratio, 4.14; 95% CI, 2.36–7.24).

Conclusions—Almost 1 in 3 patients with a diffusion-weighted magnetic resonance imaging–confirmed ischemic stroke first called the family doctor practice. Face-to-face visits to the family doctor quadrupled the odds of prehospital delay. Efforts to reduce prehospital delay should address family doctors and their staffs as important partners in the prehospital pathway.

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Prehospital delay reduces the proportion of patients with acute stroke treated with recanalization therapies. Only 10% to 20% of patients with acute stroke are treated with recanalization therapies.[1] Among those treated, the benefit from recanalization therapies decreases exponentially within hours. The number needed to treat to avoid 1 disability is 4 if intravenous thrombolysis is initiated within 1.5 hours from stroke onset, as opposed to 14 when initiated between 3 and 4.5 hours.[2] In an attempt to reduce prehospital delay, information campaigns targeting the general population have been implemented. However, a systematic review of 10 mass media interventions concluded that campaigns aimed at the public may raise awareness of stroke but do not reduce prehospital delay. Reasons for prehospital delay—especially modifiable ones—need to be better elucidated to develop novel and cost-effective interventions to reduce prehospital

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Clinical Perspective

What Is New?

- Prehospital delays are a frequent issue in patients with acute ischemic stroke and reduce the proportion of patients treated with recanalization therapies.
- The main potentially modifiable causes include (1) lack of awareness of stroke symptoms, (2) a face-to-face visit to the family doctor before hospital admission, and (3) not involving emergency medical services.
- Public education campaigns may raise awareness of stroke but do not reduce prehospital delay.

What Are the Clinical Implications?

- Newly shaped campaigns with more targets other than the public, such as family doctors and their staffs, may reduce prehospital delay.
- The campaign message is simple—do not give an appointment to a patient with stroke symptoms. Rather, instruct the patient or their proxies to immediately call emergency medical services.

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delay. This cross-sectional survey of a prospective cohort of patients with stroke aims at describing variables associated with prehospital delay among patients hospitalized with an acute ischemic stroke, confirmed by magnetic resonance imaging. In addition, we sought to explore each of the modifiable risk factors leading to prehospital delay.

Patients and Methods

This cross-sectional survey of a prospective cohort of patients with stroke was conducted at the Stroke Center of the University Hospital Basel, Switzerland. The data that support the findings of this study are available from the corresponding author upon reasonable request. Between September 1, 2015, and July 31, 2017, patients with an acute ischemic stroke, admitted to the Stroke Center of the University Hospital Basel, were consecutively enrolled in the study. All patients gave informed consent before enrollment in the study. The Stroke Center in Basel is the only acute stroke referral center of the Basler Region and surroundings, a bilingual catchment area of 350 000 people. The study was approved by the local Ethics Committee of Northwestern Switzerland, which waived written informed consent for the participation in the study.

Inclusion criteria were (1) acute ischemic stroke, defined as an acute, focal neurologic deficit with a corresponding lesion on diffusion-weighted magnetic resonance imaging; (2) hospitalization in the Stroke Center of the University Hospital Basel, Switzerland, between September 1, 2015, and July 31,

2017; and (3) at least 18 years of age. Exclusion criteria were (1) no diffusion-weighted magnetic resonance imaging available within 48 hours of admission; (2) any main diagnosis other than an acute ischemic stroke, including transient ischemic attack, defined as an acute, focal neurologic deficit of likely vascular origin but without corresponding lesion on diffusion-weighted magnetic resonance imaging; (3) incapacity to answer the structured questionnaire in the prehospital phase and no witness to the prehospital phase available to answer the structured questionnaire.

Two trained study nurses of the Clinical Trial Unit of the University of Basel, Switzerland, interviewed in person all patients or eyewitnesses along a standardized questionnaire on the prehospital phase, defined as the time between stroke onset and admission to the Stroke Center of the University Hospital Basel, Switzerland. The interviews were completed within the working day following admission. The questionnaire included questions on the time and location of stroke onset, first person contacted and delay until the first contact, first medical instance visited and delay until the first visit, awareness of stroke, education level, and with whom the patients live (the complete questionnaire is available in Data S1). All interviews were conducted at the bedside during the index hospitalization. Awareness of stroke was tested by whether the patient knew that the presenting symptoms could be attributable to a stroke. Educational level was dichotomized into academic or nonacademic. Answers were entered into a tablet computer by the study nurses during the interview. In addition to the standardized questionnaire, we documented the stroke severity on admission (National Institute of Health Stroke Scale [NIHSS] score). In place of the presence of neglect or anosognosia, we documented whether an acute ischemic injury was seen in the right hemisphere.

Statistical Analysis

To investigate the determinants of prehospital delay, the time between stroke onset—or time point of wake-up—and admission to the Stroke Center of the University Hospital Basel was stratified in 2 groups with a cutoff of 4.5 hours. We chose the time interval of 4.5 hours because it corresponds to the time window in which intravenous thrombolysis can be administered in most countries. For wake-up strokes, we chose as the relevant time point the time point of wake-up instead of last seen well because the time interval between stroke onset in sleep and awakening cannot be influenced by interventions aimed at shortening the prehospital delay. Moreover, according to the WAKE-UP (Efficacy and Safety of MRI-Based Thrombolysis in Wake-Up Stroke) trial, intravenous thrombolysis can newly be considered within 4.5 hours from wake-up.[3] Categorical variables were compared with the

Fisher exact test and continuous variables with the Mann–Whitney test. As a measure of variance for continuous variables, we report the median and interquartile range (IQR). Variables with a P value of ≤0.2 in the univariate analysis of prehospital delay were entered into a multivariate logistic regression model with prehospital delay as the end point. $P<0.05$ was deemed statistically significant. The following variables were considered potential confounders: age, stroke severity at admission measured using NIHSS, education level, living situation, knowledge level regarding stroke symptoms, a medical history (any condition such as hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation, or history of stroke), involvement of emergency medical services (EMS), and a prehospital face-to-face visit to the family doctor. All statistical tests were performed using Stata 15.1 (StataCorp LLC, College Station, TX).

Results

Overall, 336 patients were enrolled between September 1, 2015, and July 31, 2017. Patient characteristics are summarized in Table 1. Median age was 74 years (IQR, 64–81), NIHSS score on admission was 3 points (IQR, 1–5). One hundred thirty-five patients were women (40%), and before stroke 314 patients (93%) were independent in daily life (modified Rankin Scale, 0–2). One hundred forty patients (42%) arrived later than 4.5 hours and 196 patients (58%) within 4.5 hours. The median prehospital delay, that is, from stroke onset to arrival at the Stroke Center, was 3.1 hours. The median distance between the geographic location at stroke onset and the Stroke Center was 8.4 kilometers, with no significant difference between the 2 groups stratified by prehospital delay. Patients who arrived >4.5 hours after stroke onset, were more likely to be living alone (44% versus 32%; $P=0.02$), and their strokes were less severe (NIHSS 2 [IQR, 1–4] versus 3 [IQR, 1–6]; $P<0.001$; see Table 1). Whether the stroke was located in the right or left hemisphere was not associated with prehospital delay. Recanalization therapies were performed less frequently in patients arriving >4.5 hours after stroke onset compared with patients who arrived within 4.5 hours (2% versus 40%; $P<0.001$).

The first call for help was made to the family doctor in 29% (97/336). While the median NIHSS score of the patients who first called their family doctor was lower, 1 of 4 patients had an NIHSS score of 4 points or more (NIHSS, 2 [IQR, 1–4] versus NIHSS, 3 [IQR, 1–6]; $P=0.001$, in patients who called versus did not call the family doctor, respectively). Only 39% of patients (38/97) who called the family doctor were transported by EMS to the hospital, as opposed to 71% (170/239) in the rest of the cohort ($P<0.001$). Among the patients who called the family doctor, a face-to-face visit in the family practice followed in 46% (45/97). Face-to-face visits to the

family doctor were more frequent in the group with prehospital delay in comparison with the group that arrived within 4.5 hours (24% [34/140] versus 6% [11/196]; $P<0.001$). A prehospital visit to the family doctor was associated with 3 times lower odds of a recanalization therapy (9% versus 27%; $P=0.008$). Table S1 summarizes baseline characteristics among patients with and without a face-to-face visit to the family doctor.

Overall, 208 patients (62%) lacked awareness of stroke symptoms, that is, did not know that the initial symptoms could be caused by a stroke. Lack of general awareness of stroke symptoms was more frequent in patients arriving >4.5 hours after stroke onset, compared with patients who arrived within 4.5 hours (79% versus 49%; $P<0.001$, respectively). Moreover, lack of awareness was significantly more frequent among the patients with a prehospital face-to-face visit to the family doctor (78% versus 59%; $P=0.02$; see Table S1). A history of prior stroke was not associated with increased awareness of stroke symptoms. Table S2 summarizes the study population stratified by awareness of stroke symptoms.

In a multivariate analysis, a face-to-face visit to the family doctor was associated with prehospital delay (adjusted odds ratio, 4.19; 95% CI, 1.85–9.46; see Table 2). Lack of awareness of stroke symptoms was associated with higher chances of prehospital delay (adjusted odds ratio, 4.14; 95% CI, 2.36–7.24; $P<0.001$). Transport by EMS was associated with lower odds of prehospital delay by 59 percentage points (aOR, 0.41; 95% CI, 0.24–0.71; $P=0.001$). A history of preexisting illness like arterial hypertension, heart failure, diabetes mellitus, or hyperlipidemia increased the risk of prehospital delay almost 4-fold (adjusted odds ratio, 3.75; 95% CI, 1.13–12.45).

Discussion

In this cross-sectional survey of a prospective cohort of patients with stroke, a prehospital delay of >4.5 hours was observed among half of all patients with acute stroke, despite a circumscribed catchment area with a well-organized EMS in an affluent country such as Switzerland. Three modifiable risk factors were associated with prehospital delay—seeing a family doctor in the prehospital phase, lack of awareness of stroke symptoms, and transport by a means other than EMS. Unmodifiable risk factors were living alone, low baseline NIHSS score, and younger age.

Despite major advances in acute stroke care, prehospital delay has not decreased since 2006 in 26 countries, with the majority of patients failing to arrive before 3 hours.[4] Such delays contribute to the low proportion of patients with stroke receiving recanalization therapies (24% in our study). While public information campaigns are traditionally viewed as the

Table 1. Baseline Characteristics Stratified by Prehospital Delay*

	All (n=336)	Hospital Arrival Within 4.5 hours (n=196)	Hospital Arrival After 4.5 hours (n=140)	P Value
Age, y, median (IQR)	74 (64–81)	76 (64–82)	73 (61–78)	0.03[†]
Women, n (%)	135 (40)	77 (39)	58 (41)	0.74
Living at home alone before index stroke, n (%)	124 (37)	62 (32)	62 (44)	0.02[†]
Premorbid disability (mRS 3–5), n (%)	22 (7)	12 (6)	10 (7)	0.82
Academic education, n (%)	68 (20)	44 (22)	24 (17)	0.27
Private health insurance, n (%)	85 (25)	48 (24)	37 (26)	0.70
Lack of awareness of stroke symptoms, n (%)[‡]	208 (62)	97 (49)	111 (79)	<0.001[†]
NIHSS score on admission, points, median (IQR)	3 (1–5)	3 (1–6)	2 (1–4)	<0.001[†]
Wake-up stroke, n (%)	80 (24)	44 (22)	36 (26)	0.52
Acute stroke located in the right hemisphere, n (%)	135 (40)	80 (41)	55 (39)	0.82
Medical history, n (%)				
Hypertension	248 (74)	139 (71)	109 (78)	0.17
Hyperlipidemia	189 (56)	105 (54)	84 (60)	0.45
Diabetes mellitus	63 (19)	32 (16)	31 (22)	0.20
Atrial fibrillation	63 (19)	41 (21)	22 (16)	0.26
History of stroke	63 (19)	40 (20)	23 (16)	0.40
Any of the conditions above	308 (92)	175 (89)	133 (95)	0.07
Shortest route on road between geographic location at stroke onset and stroke center, kilometers, median (IQR)	8.4 (3.3–22.0)	9.3 (3.4–20.7)	6.1 (3.1–23.8)	0.39
First call/contact to, n (%)				<0.001[†]
EMS	150 (45)	114 (58)	36 (26)	
Family doctor	97 (29)	37 (19)	60 (43)	
Nonmedical personal (family)	23 (7)	14 (7)	9 (6)	
Walk-in emergency room	47 (14)	23 (12)	24 (17)	
Other	19 (6)	8 (4)	11 (8)	
Delay between stroke onset/wake-up and first call/contact, h (IQR)	0.75 (0.17–6.0)	0.25 (0.17–1.0)	10.0 (2.75–27.0)	<0.001[†]
First medical face-to-face contact, n (%)				<0.001[†]
University Hospital Basel	242 (72)	163 (83)	79 (56)	
Other hospital	44 (13)	21 (11)	23 (16)	
Family doctor	45 (13)	11 (6)	34 (24)	
Other	5 (1)	1 (<1)	4 (3)	
Transport to University Hospital Basel, n (%)				<0.001[†]
EMS	208 (62)	147 (75)	61 (44)	
Car	106 (32)	46 (23)	60 (43)	
Public transportation	18 (5)	3 (2)	15 (11)	
Walk-in emergency room	4 (1)	0	4 (3)	
Delay call to hospital arrival, h (IQR)	1.2 (0.7–2.5)	0.9 (0.6–1.4)	3.8 (1.3–10.2)	<0.001[†]
Recanalization therapy done, n (%)	82 (24)	79 (40)	3 (2)	<0.001[†]

EMS indicates emergency medical services; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

*Prehospital delay was defined as the time between stroke onset—or wake-up—and admission to the University Hospital Basel.

[†]P values indicate statistical significance ($P<0.05$).

[‡]Stroke awareness was defined by whether the patient knew that the presenting symptoms could be attributable to a stroke.

Table 2. Multivariate Regression Model Investigating the Association Between Covariates and Late Arrival (>4.5 h) at University Hospital Basel After Stroke Onset/Wake-Up

	OR	95% CI	P Value
Age	0.98	0.96–1.00	0.10
NIHSS score at admission	0.91	0.84–0.97	0.005*
Living at home alone before index stroke	1.80	1.06–3.08	0.03*
Academic education	1.19	0.61–2.31	0.62
Lack of awareness of stroke symptoms[†]	4.14	2.36–7.24	<0.001*
Hypertension	1.04	0.51–2.10	0.92
Diabetes mellitus	1.24	0.64–2.41	0.53
Atrial fibrillation	0.70	0.35–1.41	0.32
Any medical history[‡]	3.75	1.13–12.45	0.03*
Face-to-face visit to the family doctor	4.19	1.85–9.46	0.001*
Transport by EMS	0.41	0.24–0.71	0.001*

In the multivariate model, we entered variables with a *P*-value of ≤0.2 in the univariate analysis in Table 1 along with academic education. The variable "delay between stroke onset/wake-up to first call/contact" was not entered in the multivariate model because of collinearity with the variable "transport by EMS." EMS indicates emergency medical services; NIHSS, National Institute of Health Stroke Scale; OR, odds ratio.

*P values indicate statistical significance (P<0.05).

[†]Stroke awareness was defined by whether the patient knew that the presenting symptoms could be attributable to a stroke.

[‡]Any of hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation, or history of stroke.

tool to increase awareness of stroke symptoms and reduce prehospital delay, their cost-effectiveness is controversial. For instance, a cluster randomized controlled trial evaluated a stroke information campaign that included 385 television spots over 3 months and 751 000 information brochures mailed to households in northern Italy. At the end of the campaign, the proportion of patients who attributed the symptoms to stroke was significantly higher in the exposed group than in the control group. However, the proportion with hospital admission within 2 hours from stroke onset was lower in the exposed group than in the control group (38.8% versus 44.4%), as was the proportion of patients treated with intravenous thrombolysis for an ischemic stroke (22% versus 29.5%).[5] Albeit statistically nonsignificant, these differences highlight the dilemma—better awareness of stroke does not automatically translate into faster hospital admission and higher thrombolysis rates. This paradox arose also in a meta-analysis of 6 information campaigns aimed at the public only: The information campaigns increased awareness of stroke symptoms but not of the need for emergency response.[6] On a population level, the positive effect on increased awareness seems to be only transient, with decreasing awareness as soon as 5 months after the end of 2 primetime television

campaigns conducted in Ontario, Canada, whose costs amounted to $3.67 million.[7]

Family physicians and their staffs were the first responders for one third of patients, a relevant proportion of the overall cohort. The instruction to be delivered over the phone to patients with suspected stroke is to immediately call EMS to reach the next hospital. Reality proved different. A face-to-face visit occurred in one half of patients who called, which quadrupled the odds of prehospital delay. EMS was called only by 39% of the patients who first contacted the family physician. This is likely to have jeopardized the chances of a recanalization therapy among eligible patients, as an NIHSS score of ≥4 points was present in 1 of 4 patients who called the family physician. Previous studies identified an association between a visit to a family doctor and prehospital delay, but they did not analyze separately the initial call to the family doctors and the subsequent face-to-face visit (if it took place), nor did these studies adjust for NIHSS score.[8–19]

In our study, a preexisiting illness such as diabetes mellitus or heart failure increased the risk of prehospital delay almost 4-fold. Patients with stroke with a history of a prior stroke, that is, the index stroke was not their first stroke, did not prove to be more aware of stroke symptoms than patients with a first-ever stroke. As yet, educational information provided during hospitalization has been left to the discretion of the treating team. Structured information provided at hospital discharge or during consultations in family practices about recognizing stroke symptoms and the importance of avoiding prehospital delays deserve to be evaluated as a possibly more cost-effective alternative to public mass campaigns.

In our study, living alone was associated with higher chances of prehospital delay, a finding in line with prior studies.[20] Median delay between stroke onset and call for medical assistance was 3 times higher among patients living alone (60 minutes versus 20 minutes). Independent of stroke severity, living alone almost doubled the probabilities of prehospital delay. In the future, wearable technologies (eg, smartwatches) may shorten the delay between stroke onset and call for help.

Our study has strengths and limitations. Strengths include the prospective study design and patient selection based on positive magnetic resonance diffusion-weighted imaging, which allowed exclusion of mimics of ischemic stroke. Trained study nurses conducted bedside interviews of patients and proxies along a standardized tablet-based questionnaire. As a limitation, this study was conducted in a single center, limiting the generalizability of our results. However, the catchment area includes 350 000 people spread over 2 language regions (Swiss German and Swiss French), which increases the diversity of the population. Second, the reasons for poor

awareness of stroke symptoms in patients with a history of stroke remain unclear, as well as the potential role of proxies with a history of stroke in reducing prehospital delay. Overall, patients with severe strokes were underrepresented, given their incapacity to answer the questionnaire or lack of proxies. Despite the low median NIHSS score, the overall rate of recanalization therapies of 24% argues that neurological deficits were often deemed severe enough to limit activities of daily life.

In conclusion, our findings can contribute to shaping new campaigns aimed at reducing prehospital delay. Targeting family doctors and their staffs may reduce prehospital delay. The campaign message is simple—do not give an appointment to a patient with stroke symptoms. Rather, instruct the patient or their proxies to immediately call EMS.

Sources of Funding

Disclosures

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SUPPLEMENTAL MATERIAL

Data S1.

Reasons for Prehospital Delay in Acute Ischemic Stroke - Questionnaire

SC: Single Choice, i.e. only one answer is possible
MC: Multiple Choice, i.e. multiple answers are possible

1. **(SC) Where were you at the time of symptom onset?**
   - country (Dropdown Menu with all countries of the world [Switzerland and neighboring countries on top])
   - zipcode (if referred via ambulance: ambulance protocol)
   - street address (if referred via ambulance: ambulance protocol)

2. **(SC) The address of question #1 is**
   - your place of residence →if not: indicate residential address
   - place of employment
   - public place (e.g. restaurant, movies, street)
   - holiday domicile
   - other

3. **(SC) Is the time of symptom onset known?**
   - Yes: DD.MM.YYYY um XX:YY
   - No: the patient was last seen well on DD.MM.YYYY at XX:YY (e.g. bedtime)

4. **(MC) What activity did you pursue at the time of symptom onset?**
   - physical activity (e.g. household, walking, sport, shopping)
   - sitting position (e.g. computer, reading, television, desk work, eating)
   - sleep
   - urinating/defecation
   - sexual intercourse (+/- 30 minutes)
   - consumption of illicit drugs or alcohol (+/- 30 minutes)
   - other + free text

5. **(MC) Who was present at the time of symptom onset?**
   - nobody
   - partner
   - family members
   - acquaintances/neighbors/friends
   - strangers/passers-by
   - nursing staff (e.g. of nursing home)
   - other + free text

6. **(SC) Who first realized that there was something amiss?**
   - patient him/herself
   - partner
   - relatives
   - friends or acquaintances
   - passers-by
   - other + free text

7. **(SC) Did you know what a stroke is?**
   - Yes/No

8. **(SC) Did you know the symptoms could be caused by a stroke?**
   - Yes: how did you know? (general education /internet/relatives/media)
   - No + free text what did you consider?

9. **(SC) What kind of help did you primarily seek?**
   - 911/ambulance
   - family doctor
   - internet, medical literature
   - non-medical personnel (e.g. family members)
   - advice by telephone (e.g. MedGate)

10. **(SC) Who primarily made contact to call for help (e.g. 911)?**
    - patient him/herself
    - relatives
    - friends/acquaintances
    - eyewitness/passers-by/other

11. **(SC) How many hours and minutes passed from the time of symptom onset and the first contact with the ambulance or a family doctor?**
    - XX:YY
    - unknown/ not assessable

12. **(MC) Why did you not call the ambulance earlier or why did you not call the ambulance at all?**
    - not applicable (call within 15 min of symptom onset)
    - hope that symptoms will resolve spontaneously
    - afraid of calling the ambulance unnecessarily / „not meaning to disturb"
    - feelings of shame
    - fear of the costs
    - inability to call the ambulance due to stroke (e.g. aphasia)
    - inability to call the ambulance due to technical issues (e.g. no cellphone reception)

13. **(SC) Are you capable of using a cellphone or telephone?**
    - Yes, it is possible without reading aid
    - Yes, but I need a reading aid
    - No

14. **(SC) Can you correctly indicate the emergency telephone number in Switzerland?**
    - 911 is correctly indicated
    - 911 is not indicated, although the faculty of speech is not impaired (e.g. the wrong number is indicated)
    - 911 is not indicated, due to an impaired faculty of speech

15. **(SC) What medical institution were you taken to/did you approach first? (Please abstract from *Ismed* or the medical records)**
    - University Hospital Basel
    - other hospital
      - At Choice: Liestal, Bruderholz, Delémont, other hospital in Switzerland, other hospital in Europe, other hospital in America, other hospital in Asia, other Hospital in Oceania, other hospital in Africa
    - family doctor→zipcode
    - other →please specify in free text

16. **(SC) What means of transport did you reach the first hospital with? (Please abstract from *Ismed* or the medical records)**
    - ambulance with sirene (as stated in the ambulance protocol)
    - ambulance without sirene (as stated in the ambulance protocol)
    - helicopter/airplane

- private car as co-driver
- private car as driver
- taxi
- means of public transport
- on foot
- already hospitalized at the time of symptom onset
- other + free text

Only if question #16 is answered with with answer 1, 2 or 3:

a. Emergency call and arrival of the ambulance: XX min (PD Matthias Zürcher, minimum dataset for all operations) + ambulance protocol

b. Arrival of the ambulance and departure toward the first hospital (on-scene time): XX min (PD Matthias Zürcher, minimum dataset for all operations)

c. Departure from place of action and arrival at the first treating hospital: XX min (PD Matthias Zürcher, minimum dataset for all operations)

17. (SC) Do you have a family doctor you saw within the last 5 years?
- Yes, I saw him/her within the last 5 years
- Yes, but I didn't see him/her within the last 5 years
- No, in case of health problems I go to the emergency room
- No, in case of health problems I go to a walk-in clinic
- No, in case of health problems I seek help otherwise (i.e.) + free text
- not specified

18. (SC) What is your civil status?
- unmarried
- married
- divorced
- widowed

19. (SC) What is your highest educational achievement confirmed by a certificate or diploma? *[do not read out, allocate]*
- did not attend a school
- did not graduate mandatory school
- graduated solely mandatory school
- one-year training: 10. grade/vocational school/preliminary course/language school with certificate/academic year domestic management/bridging program
- two-year basic training: swiss federal vocational certificate (EBA)
- two-year training: full-time vocational school, commercial school
- two-to-three-year training: school of general education
- three-to-four-year voctional education, dual vocational education and training with swiss federal VET diploma
- three-to-four-year full-time vocational school, apprenticeship workshop, commercial school
- Teaching staff seminar
- higher education entrance qualification
- Swiss Federal Vocational Baccalaureate
- higher vocational training with swiss federal diploma
- higher professional school (two-year full-time or three-year part-time)
- higher professional school of engineering (three-year full-time or four-year part-time)
- College (FH)
- College of educatiion (PH)
- University, ETH
- I do not know/not specified
- other + free text

20. (SC) Are you swiss-born?
- Yes/No

* not specified

21. (SC) Ethnicity of the patient
* Caucasian
* Asian
* Black-AfricanSchwarz-afrikanisch
* mutiple Etnicities

22. (SC) Only if question #20 was answered with „no"; When did you come to Switzerland?
* _____ enter year
* I don't know / not specified

23. (SC) Are you swiss, foreigner or dual citizen?
* Swiss
* Foreign nationality   continue with question 24
* Swiss dual citizen   continue with question 24
* stateless
* not specified

24. (MC) What is your nationality? *(3 possible answers. In case of 2 or 3 nationalities, indicate order of acquisition)*
* enter exact nationality
* not specified

25. (SC) What are your living conditions?
* living alone
* living together
* institutionalized

26. (SC) What is your health insurance model?
* ordinary with franchise
* HMO
* prior advice by telephone
* other + free text

27. (SC) What is your class of insurance?
* general insurance / (3. class)
* semiprivate / (2. class)
* private / (1. class)

Table S1. Baseline Characteristics in Patients With and Without Face-to-Face Visit to the Family Doctor.

	All (n=336)	Face-to-Face to the Family Doctor (n=45)	NO Face-to-Face to the Family Doctor (n=291)	p
Age, years, median (IQR)	74 (64 – 81)	75 (66-83)	74 (63-81)	0.27
Women, n (%)	135 (40)	21 (47)	114 (39)	0.41
Living at home alone prior to index stroke, n (%)	124 (37)	18 (40)	106 (36)	0.81
Premorbid Disability (mRS 3-5), n (%)	22 (7)	1 (2)	21 (7)	0.33
Academic education, n (%)	68 (20)	1 (2)	67 (23)	**<0.001**
Private health insurance, n (%)	85 (25)	11 (24)	74 (25)	1.0
Lack of awareness of stroke symptoms, n (%)	208 (62)	35 (78)	173 (59)	**0.02**
NIHSS admission, points, median (IQR)	3 (1-5)	2 (1-5)	3 (1-6)	0.49
Wake-up Stroke	80 (24)	10 (22)	70 (24)	0.85
Medical History, n (%)				
Hypertension	248 (74)	38 (84)	210 (72)	**0.10**
Hyperlipidemia	189 (56)	27 (60)	162 (56)	0.22
Diabetes mellitus	63 (19)	9 (20)	54 (19)	0.84
Atrial fibrillation	63 (19)	7 (16)	56 (19)	0.68
History of stroke	63 (19)	7 (16)	56 (19)	0.68
Any of the above conditions	308 (92)	43 (96)	265 (91)	0.4
First call/contact to:				**<0.001**
Ambulance	150 (45)	1 (2)	149 (51)	
Family Doctor	97 (29)	40 (89)	57 (20)	
Non-medical personal (family)	23 (7)	2 (4)	21 (7)	
Walk-in Emergency Room	47 (14)	0 (0)	47 (16)	
Other	20 (6)	2 (4)	18 (6)	
Delay between stroke onset/wake-up and first call/contact, h (IQR)	0.75 (0.17-6.0)	11 (1.75-35.5)	0.38 (0.17-2.5)	**<0.001**
Transport to University Hospital Basel, n (%)				**0.002**
EMS	208 (62)	17 (38)	191 (66)	
Car	106 (32)	22 (49)	84 (29)	
Public transportation	18 (5)	5 (11)	13 (4)	
Walk-in Emergency Room	4 (1)	1 (2)	3 (1)	
Delay Call to Hospital Arrival, h (IQR)	1.2 (0.7-2.5)	2.3 (1.2-6.7)	1.1 (0.7-1.9)	**<0.001**
Recanalization Therapy done, n (%)	82 (24)	4 (9)	78 (27)	**0.008**

IQR = Interquartile range; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale

Table S2. Baseline characteristics in Patients With and Without Stroke Awareness*.

	All (n=336)	Awareness of stroke symptoms (n=128)	NO awareness of stroke symptoms (n=208)	*p*
Age, years, median (IQR)	74 (64 – 81)	74 (63-80)	74 (64-81)	0.91
Women, n (%)	135 (40)	49 (38)	86 (41)	0.65
Living at home alone prior to index stroke, n (%)	124 (37)	43 (34)	81 (39)	0.35
Premorbid Disability (mRS 3-5), n (%)	22 (7)	9 (7)	13 (6)	0.82
Academic education, n (%)	68 (20)	36 (28)	32 (15)	**0.008**
Private health insurance, n (%)	85 (25)	50 (24)	35 (27)	0.52
NIHSS admission, points, median (IQR)	3 (1-5)	3 (1-5)	3 (1-5)	0.92
Wake-up Stroke, n (%)	80 (24)	34 (27)	46 (22)	0.36
Medical History, n (%)				
Hypertension	248 (74)	94 (73)	154 (74)	0.90
Hyperlipidemia	189 (56)	66 (52)	123 (59)	0.21
Diabetes mellitus	63 (19)	15 (12)	48 (23)	**0.01**
Atrial fibrillation	63 (19)	20 (16)	43 (21)	0.31
History of stroke	63 (19)	30 (23)	33 (16)	0.09
Any medical history	308 (92)	118 (92)	190 (91)	0.84
First call/contact to:				0.21
EMS	150 (45)	65 (51)	85 (41)	
Family Doctor	97 (29)	34 (27)	63 (30)	
Non-medical staff (family)	23 (7)	6 (5)	17 (8)	
Walk-in Emergency Room	47 (14)	19 (15)	28 (13)	
Other	19 (6)	4 (3)	15 (7)	
Delay between stroke onset/wake-up and first call/contact, h (IQR)	0.75 (0.17-6.0)	0.33 (0.17-2.0)	1.0 (0.17-10.0)	**0.002**
First medical face-to-face contact, n (%)				0.11
University Hospital Basel	242 (72)	98 (77)	144 (69)	
Other Hospital	44 (13)	18 (14)	26 (13)	
Family Doctor	45 (13)	10 (8)	35 (17)	
Other	5 (1)	2 (2)	3 (1)	
Transport to University Hospital Basel, n (%):				0.47
EMS	208 (62)	86 (67)	122 (59)	
Car	106 (32)	36 (28)	70 (34)	

Public transportation	18 (5)	5 (4)	13 (6)	
on foot	4 (1)	1 (<1)	3 (1)	
in-hospital	1 (<1)	1 (<1)	0	
Delay Call to Hospital Arrival, h (IQR)	1.2 (0.7-2.5)	1.0 (0.6-1.6)	1.3 (0.8-3.8)	**0.003**
Time between stroke onset/wake-up to Hospital arrival, h (IQR)	3.1 (1.3 – 11)	2.1 (1.1 – 4.1)	5.2 (1.5 – 18.1)	**<0.001**
Recanalization Therapy done, n (%)	82 (24)	37 (29)	45 (22)	0.15

*Stroke Awareness was defined by whether or not the patient knew that the presenting symptoms could be due to a stroke.

IQR = Interquartile range; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale.