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Effect of admission time on provision of acute stroke treatment at stroke units and stroke centers—An analysis of the Swiss Stroke Registry

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Abstract

Introduction: Rapid treatment of acute ischemic stroke (AIS) depends on sufficient staffing which differs between Stroke Centers and Stroke Units in Switzerland. We studied the effect of admission time on performance measures of AIS treatment and related temporal trends over time.

Patients and methods: We compared treatment rates, door-to-image-time, door-to-needle-time, and door-to-groin-puncture-time in stroke patients admitted during office hours (Monday–Friday 8:00–17:59) and non-office hours at all

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certified Stroke Centers and Stroke Units in Switzerland, as well as secular trends thereof between 2014 and 2019, using data from the Swiss Stroke Registry. Secondary outcomes were modified Rankin Scale and mortality at 3 months.
Results: Data were eligible for analysis in 31,788 (90.2%) of 35,261 patients. Treatment rates for IVT/EVT were higher during non-office hours compared with office hours in Stroke Centers (40.8 vs 36.5%) and Stroke Units (21.8 vs 18.5%). Door-to-image-time and door-to-needle-time increased significantly during non-office hours. Median (IQR) door-to-groin-puncture-time at Stroke Centers was longer during non-office hours compared to office hours (84 (59–116) vs 95 (66–130) minutes). Admission during non-office hours was independently associated with worse functional outcome (1.11 [95%CI: 1.04–1.18]) and increased mortality (1.13 [95%CI: 1.01–1.27]). From 2014 to 2019, median door-to-groin-puncture-time improved and the treatment rate for wake-up strokes increased.
Discussion and Conclusion: Despite differences in staffing, patient admission during non-office hours delayed IVT to a similar, modest degree at Stroke Centers and Stroke Units. A larger delay of EVT was observed during non-office hours, but Stroke Centers sped up delivery of EVT over time. Patients admitted during non-office hours had worse functional outcomes, which was not explained by treatment delays.

Keywords
Stroke, admission time, service provision, outcome, quality of care

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Introduction

Intravenous thrombolysis (IVT) and endovascular recanalization therapy (EVT) reduce disability in patients with acute ischemic stroke (AIS).[1,2] Rapid delivery of treatment is crucial and depends – among other factors – on the presence of experienced staff and access to infrastructure. In addition, acute stroke care has become more and more complex due to recent extension of time windows and imaging eligibility criteria in both IVT- and EVT-treated patients.[3,4] Furthermore, according to most stroke guidelines patients presenting with so called wake-up strokes can also benefit from acute reperfusion therapies depending on certain imaging features.[5–7] These aspects represent a considerable challenge for staff involved in the acute treatment of AIS.

However, staff levels and availability of infrastructure may vary depending on time of the day and day of the week, and differ between Stroke Centers and Stroke Units. In Switzerland, certification guidelines require a 24/7 attendance of a stroke neurologist at Stroke Centers whereas an on-call service is permitted at night and on weekends at Stroke Units following the guidelines of the *European Stroke Organization*.[8] While both, Stroke Centers and Stroke Units, deliver IVT and provide continuous physiological monitoring, EVT is exclusively performed in Stroke Centers in Switzerland. Understanding the effect of day and time of admission on delivery and functional outcome of acute stroke care is relevant for service providers and health policy makers.

Previous research on the effect of admission during "office-hours" versus "non-office hours" on the speed of delivery and outcomes of IVT was done in heterogeneous settings and yielded controversial results.[9–13] Importantly, most of the previous research investigated patient cohorts when neither EVT per se, nor reperfusion treatment for AIS in the extended time window were widely implemented in everyday practice. The increasing proportion of stroke patients receiving EVT poses greater demands on staff and infrastructure.

In order to consolidate and extend the evidence on diurnal and weekday variations of acute stroke treatment and to examine possible changes following recent modifications in therapeutic concepts, we conducted the present study using prospectively collected data from the Swiss Stroke Registry (SSR) between 01/2014 and 12/2019.

Methods

All data and materials can be accessed by request from the corresponding author (leo.bonati@usb.ch).

Study design

For this cohort study, we used prospectively collected data from the *Swiss Stroke Registry* (SSR). The SSR is a national web-based registry designed to facilitate multi-centric research in acute stroke and assure the provision and quality of acute stroke care in Switzerland, which started in January 2014.[14] The registry collects a standardized dataset of all patients with acute stroke, TIA and other acute cerebrovascular events including a follow-up assessment after 3 months. The registry is compulsory for all hospitals certified as Stroke Units or Stroke Centers in Switzerland, in line with the *European Stroke Organization* criteria.[15] The database is managed by the Clinical Trial Unit (CTU) of the University of Basel. Data collection is done locally in each

Stroke Center/each Stroke Unit. All patients with ischemic stroke admitted between 01.01.2014 and 31.12.2019 were included.

Parameters of interest for the present study were age, sex, National Institutes of Health Stroke Scale (NIHSS) score,[16] date and time of stroke onset (or last seen well), of hospital admission, of first image and of treatment initiation (IVT and/or EVT), presence of wake up stroke, blood pressure prior to IVT treatment, glucose levels in blood serum on admission, vascular risk factors according to predefined criteria[17] and prior treatment with anticoagulation as well as pre-stroke functional status measured by the modified Rankin Scale (mRS).[18] Wake-up stroke is defined as a stroke with symptoms that were present when the patient awoke but not prior to falling asleep. Clinical data, neurologic and functional outcomes during hospitalization and at 3 months after stroke were also collected. Clinical evaluations, as well as NIHSS and mRS assessments, were performed by certified stroke neurologists as part of their clinical activity. If an in-person visit was not possible at 3 months, mRS score was assessed by a phone interview with mRS-trained examiners.

Outcomes

Primary outcomes were the rate of patients with acute reperfusion therapy (i.e., the proportion of patients with AIS receiving IVT and/or EVT) and in-hospital performance measures in patients receiving IVT and/or EVT), defined as the following time intervals: (i) from hospital admission to brain imaging in IVT/EVT ("door-to-image-time" (DIT)) (ii) from hospital admission to start of IVT ("door-to-needle time" (DNT)) (iii) from hospital admission to start of EVT ("door-to-groin-puncture time" (DPT)). As secondary outcomes, we investigated functional status defined by the mRS, as well as mortality at 3 months.

Statistical analyzes

Statistical analyzes were performed with R version 3.6.3 (*R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/*). The database is implemented in the commercial software secuTrial (interActive Systems GmbH, Germany) and is managed by the Clinical Trial Unit (CTU) of the University of Basel aided by the secuTrialR package.[19]

We investigated differences in primary and secondary outcomes between patients admitted during "office hours" (OH) (Monday–Friday 8:00–17:59) and patients admitted during "non-office hours" (NH) (Monday–Friday 18:00–07:59, Saturday, Sunday, national holidays), at Stroke Centers and Stroke Units separately. Continuous data were summarized as median and interquartile range (IQR). We compared the rates of acute reperfusion therapy using Chi^2-test and the performance measures using Wilcoxon test. Performance measures during OH and NH were additionally compared using a linear mixed model where the respective center was included as random effect. Performance measures were log-transformed to better meet the normality assumption.

In a subgroup, the association between admission time and functional outcome as well as mortality was estimated by calculating odds ratios (OR) with 95% confidence intervals (95% CI), using ordered logistic regression models and binary logistic regression, respectively. Analyses were done both unadjusted and adjusted for baseline NIHSS, age, pre-stroke mRS, and stroke-onset-to-treatment time (for patients receiving acute reperfusion therapy). Patients with missing data on the mRS at 3 months were excluded from this subanalysis. Furthermore, we evaluated the change over time from 2014 until 2019 regarding in-hospital performance measures (DIT, DNT, DPT) to investigate any learning curve effects in Stroke Units and Stroke Centers separately in descriptive analyzes. Performance measures displayed as median and IQR were analyzed each year beginning in 01/2014. Patients referred to hospital with symptoms of wake-up stroke as well as patients with in-hospital strokes were excluded from these analyses.

As an exploratory analysis, we also investigated the rate of patients treated with IVT or EVT for wake-up strokes for each year.

Role of the funding source/ethics

No sponsor was involved in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

The study complied with the Declaration of Helsinki. The study was classified as a Quality Assurance Study by the responsible ethics committee and the necessity for formal review was waived. In accordance with national law, patients were informed about the use of their routinely collected data for research purposes. Patients who denied use of their data were excluded from the analysis. Anonymized data will be shared on request from any qualified investigator. The analysis code is available on GitHub: https://github.com/PatrickRWright/Publications_code

Results

Data were eligible for analysis in 31,788 (90.2%) of 35,261 AIS patients. Reasons for excluding patients were missing data on DIT, DNT or DPT ($n = 3473$; 9.8%).

Baseline characteristics

In Stroke Centers, 11,844 patients (48.7%) were admitted during office-hours (OH) and 12,471 (51.3%) during

Table 1. Baseline characteristics of all ischemic stroke patients.

	Stroke center		Stroke unit	
	Office hours	Non-office hours	Office hours	Non-office hours
Patients, *n* (%)	11,844 (48.7)	12,471 (51.3)	3919 (52.4)	3554 (47.6)
Demographics				
Age, years, median [IQR]	75 [65–83]	75 [63–83]	76 [66–84]	75 [63–83]
Male sex, *n* (%)	6739 (57.0)	7145 (57.4)	2170 (55.5)	2036 (57.3)
Independent prior to stroke (pre-mRS 0–2), median[IQR]	9091 (88.1)	9745 (88.9)	2909 (89.3)	2657 (90.0)
Stroke characteristics				
NIHSS, median [IQR]	4 [1–9]	4 [2–11]	3 [1–6]	3 [1–7]
NIHSS, patients with acute reperfusion therapy, median [IQR]	9 [4–16]	9 [5–16]	6 [3–11]	6 [4–12]
Onset-to-admission time, min, median [IQR]	276 [86–982]	208 [81–645]	510 [108–1330]	238 [85–766]
Medical history				
Hypertension, *n* (%)	8676 (74.7)	8996 (73.5)	2863 (76.9)	2560 (75.9)
Diabetes mellitus, *n* (%)	2347 (20.2)	2495 (20.4)	802 (21.5)	752 (22.3)
Coronary artery disease, *n* (%)	2040 (17.7)	2217 (18.2)	598 (16.8)	610 (18.8)
Atrial fibrillation, *n* (%)	3031 (24.8)	2791 (24.0)	816 (22.0)	779 (23.2)
Prior stroke, *n* (%)	2168 (18.7)	2274 (18.6)	657 (17.7)	617 (18.3)
Systolic blood pressure, mmHg, median [IQR]	153 [137–172]	155 [138–175]	160 [140–180]	160 [141–180]
Glucose, mmol/l, median [IQR]	6.3 [5.5–7.6]	6.5 [5.7–7.9]	6.3 [5.5–7.6]	6.5 [5.7–8.0]
Medication				
Prior anticoagulation, *n* (%)	1755 (21.7)	1872 (22.0)	486 (17.8)	477 (19.5)

non-office hours (NH). In Stroke Units, 3919 (52.4%) arrived during OH and 3554 (47.6%) during NH. Overall, there was no substantial difference in characteristics of AIS patients arriving during OH and those arriving during NH: age, sex, stroke severity, pre-stroke disability as well as the prevalence of cardiovascular risk factors were similar between groups. Stroke-onset-to-admission time was higher during OH in Stroke Centers and Stroke Units (Table 1). Among patients receiving acute reperfusion therapy, baseline characteristics were evenly distributed (Supplemental Table I).

Patients in Stroke Centers had higher baseline stroke severity, were more likely to suffer from atrial fibrillation and more frequently under anticoagulation at the time of their stroke than patients treated in Stroke Units (Table 1).

The baseline characteristics of the excluded AIS patients are presented in Supplemental Table II. 378 (10.9%) of the excluded patients received acute reperfusion therapy.

Primary outcomes: Rate of acute reperfusion therapy and in-hospital performance measures

Patients with AIS arriving during NH at Stroke Centers received acute reperfusion therapy with IVT or EVT more often than during OH (40.8% vs 36.5%, $p < 0.001$). Likewise, patients being admitted during NH to Stroke Units were more likely to be treated with IVT than during OH (NH 21.8% vs OH 18.5%, $p < 0.001$) (Table 2).

Median DIT in patients treated with acute reperfusion therapy was faster during OH: Stroke Centers, DIT 23 vs 22 minutes, $p < 0.001$; Stroke Units, DIT 19 vs 17 minutes; $p < 0.01$. Fittingly, median DNT was significantly increased in patients arriving during NH compared to arriving during OH, both at Stroke Centres (43 vs 37 minutes, $p < 0.001$) and Stroke Units (45 vs 39 minutes, $p < 0.001$). Median DPT at Stroke Centres was longer in patients arriving during NH compared to OH (95 vs 84 minutes, $p < 0.001$) (Table 2).

The time differences between OH and NH for each primary outcome remained significant after calculating a linear mixed model with Stroke Center or Stroke Unit included as random effect (Supplemental Table III).

Secondary outcomes: Functional outcome and mortality

The mRS at 3 months was missing in 7489 AIS patients (23.6%, 5332 Stroke Center patients and 2157 Stroke Unit patients). After adjustment for age, baseline NIHSS, pre-stroke mRS and acute reperfusion treatment, AIS patients arriving during NH in Stroke Centers had 1.11 (95% CI 1.04–1.18) times the odds of having a worse functional outcome at 3 months and OR 1.13 (95% CI 1.01–1.27) times the odds for mortality at 3 months compared with arriving during OH. Admission during NH in Stroke Units also increased the odds for worse functional outcome (1.12 (95%

Table 2. Thrombolysis rate and performance measures.

		Office hours	Non-office hours	Office vs non-office hours, *p*-value
Acute reperfusion therapy, *n* (%)†	Stroke Center	4322 (36.5)	5090 (40.8)	<0.001
	Stroke Unit	724 (18.5)	773 (21.8)	<0.001
Door-to-image time, min, median (IQR)‡	Stroke Center	22 (16–30)	23 (17–31)	<0.001
	Stroke Unit	17 (11–25)	19 (13–27)	<0.01
Door-to-IVT time, min, median (IQR)	Stroke Center	37 (27–54)	43 (30–61)	<0.001
	Stroke Unit	39 (29–53)	45 (32–65)	<0.001
Door-to-EVT time, min, median (IQR)	Stroke Center	84 (59–116)	95 (66–130)	<0.001

†Including wake-up strokes.
‡In patients treated with acute reperfusion therapy.

Table 3. Multivariable analysis of outcomes. Odds ratio (95% confidence interval), *p*-value.

			Worse outcome	Mortality
All ischemic stroke patients†	Non-office hours vs office hours	Stroke Center	1.11 (1.04–1.18)† $p=0.002$	1.13 (1.01–1.27)† $p=0.037$
		Stroke Unit	1.12 (0.99–1.27)† $p=0.061$	1.17 (0.90–1.52)† $p=0.243$
Ischemic stroke patients with acute reperfusion therapy‡	Non-office hours vs office hours	Stroke Center	1.18 (1.07–1.31)‡ $p<0.001$	1.18 (1.01–1.38)‡ $p=0.034$
		Stroke Unit	1.12 (0.87–1.46)‡ $p=0.374$	1.48 (0.89–2.47)‡ $p=0.131$

†Age, baseline NIHSS, pre-mRS, acute reperfusion treatment.
‡Age, baseline NIHSS, pre-mRS, onset-to-treatment time.

CI 0.99–1.27)) and mortality (1.17 (95% CI 0.90–1.52)) at 3 months without reaching statistical significance.

Among patients receiving acute reperfusion therapy, admission during NH was again associated with worse outcome (1.18 (95% CI 1.07–1.31)) and mortality (1.18 (95% CI 1.01–1.38)) at 3 months in Stroke Centers, after adjustment for patient characteristics and onset-to-treatment time. At Stroke Units, arrival during NH increased the point estimate similarly for worse outcome (1.12 (95% CI 0.87–1.46)) and mortality (1.48 (95% CI 0.89–2.47)) without reaching statistical significance (Table 3, Figure 1).

Temporal trends in performance measures and treatment of wake-up strokes

The median DIT for patients with acute reperfusion therapy remained relatively constant from 2014 to 2019 at Stroke Centers and Stroke Units. Similarly, the median DNT remained relatively stable (Stroke Center: 2014 39 vs 2019 40 minutes; Stroke Unit: 2014 38 vs 2019 40 minutes). However, a considerable decrease of DPT at Stroke Centers (2014 112 vs 2019 84 minutes) over time became apparent (Figure 2).

The probability for acute reperfusion treatment of wake-up stroke with IVT and/ or EVT increased over time from 13.2% in 2014 to 25.0% in 2016, and to 31.7% in 2019 (Figure 3).

Discussion

In our study population about 50% of all ischemic stroke patients were admitted during NH, where the rate of acute reperfusion therapy (IVT or EVT) turned out to be higher than during OH, both at Stroke Centers (40.8% vs 36.5%) and Stroke Units (21.8% vs 18.5%). We observed that AIS patients were admitted considerably faster during NH than during OH, which may have contributed to the higher reperfusion therapy rate.

We found a statistically significant delay in delivery of IVT during NH, both at Stroke Centers and Stroke Units. Previous studies on diurnal variations of service provision in acute stroke treatment have yielded inconsistent results: A Swedish study found that DNT within 30 minutes was less likely during NH.[12] In line, Reuter et al. found the longest DNT time and the lowest IVT rate between 03:01 and 06:00 am.[9] Furthermore, Kristiansen et al. found in-hospital performance measures to be worse in patients admitted during NH.[20] Other studies, however, showed no association of DNT with time of hospital arrival[11] and no deterioration of acute reperfusion therapy rates in candidates for thrombolytic therapy.[21]

Differences in staffing of emergency and radiology departments (independent of acute stroke services) might contribute to the higher DNT during NH by delaying image acquisition and decision-making.[12] However, the delays in

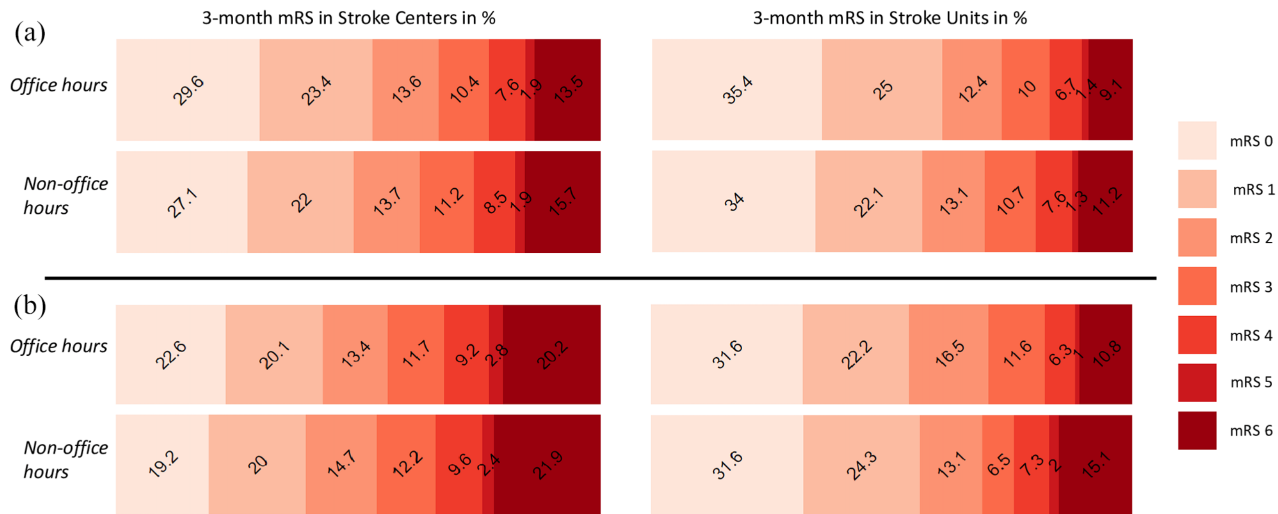

Figure 1. Modified Rankin Scale (mRS) at 3 months. (a) mRS at 3 months in all ischemic stroke patients. (b) mRS at 3 months in ischemic stroke patients treated with acute reperfusion therapy.

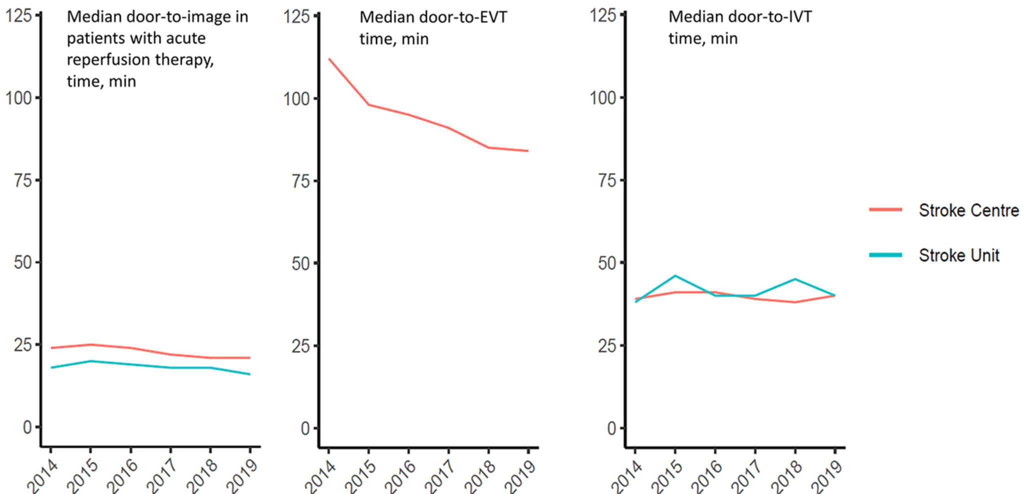

Figure 2. Performance measures over time (years).

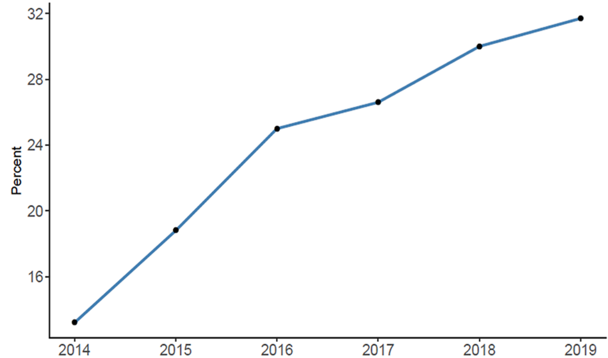

Figure 3. Rate of wake-up strokes with acute reperfusion treatment.

DIT in the present study during NH were very minor. Some studies have also reported that patients admitted during NH may have more severe strokes and more comorbidities, potentially rendering treatment decisions more difficult.[12,22] Yet in our study, baseline characteristics regarding comorbidities and stroke severity were well balanced between patients arriving during OH and NH. As there is little difference in DIT between NH and OH, the procedural step most sensitive to delay DNT during NH appears to be the decision whether to administer IVT. In Stroke Units the treating physician is obliged to make contact with the on-call neurologist during NH which takes additional time. In Stroke Centers, certification criteria in Switzerland require a 24/7 presence of a stroke neurologist. Despite these differences in staff requirements, the delay in DNT during NH compared

with OH was similar at Stroke Centers and Stroke, and only moderate in extent. It has to be noted that patients admitted to Stroke Centers for IVT were more likely to take oral anticoagulation than patients treated at Stroke Units, which may cause additional delays in treatment during NH, depending on the availability of coagulation tests.

Regarding the speed of EVT at Stroke Centers, we found a substantial, 11 minute in-house treatment delay during NH compared with admission during OH. One previous study analyzing data from 2013 to 2014 found longer door-to-reperfusion times for patients admitted during night-time and weekends.[23] Another study reported significantly longer image-to-treatment times during NH.[24] Recently, it was suggested that EVT in the morning is associated with good and EVT at the end of the workday with poor functional outcome.[25] In the same study DPT was also increased during night-time. Optimizing EVT performance during NH is crucial because it has already been suggested that the majority of EVTs occur during NH, when transfer to hospital was reported to be delayed.[24,26] EVT is a staff-intensive procedure that requires presence of nurses, medical technical assistants, anesthesiologists and neurointerventionalists. Furthermore, during NH the neurointerventionalist and other on-call staff have to travel to the hospital from home, in most settings.[27] Overall, we observed a clear reduction in DPT over the years, indicating that Stroke Centers have continuously optimized their in-house procedures to deliver EVT (Figure 2). The same secular trend could not be observed for DNT, possibly indicating a certain ceiling effect in the way that IVT pathways were already optimized at the beginning of the capture period. In Stroke Units DNT showed fluctuations over time with increases in 2015 and 2018. Thus, counteracting trends prolonging DNT must also be considered, such as the increasing proportion of patients on oral anticoagulation receiving IVT after emergency coagulation checks (which take time).[28] Over time, DIT remained stable with no considerable fluctuations suggesting that DIT was close to optimal already or that some gains are still possible. Furthermore, Stroke Centers and Stroke Units appear to have quickly adopted the recent evidence and treatment recommendations for wake-up stroke, indicated by a more than doubling in the proportion of patients with wake-up stroke receiving acute recanalization therapy from 2014 to 2019 (Figure 3).

Admission during NH resulted in higher odds for worse outcome and mortality in ischemic stroke patients similar to other studies investigating outcomes of patients suffering from AIS as well as other diseases during NH.[12,13,29] Regarding EVT one study found no association between patients receiving EVT during the weekend and in-hospital death or functional status at discharge while in another study patients who were treated with EVT in nonteaching hospitals during the weekend had worse functional status at discharge.[30,31] However, these studies only distinguished between weekend and weekdays and outcome measures were in-hospital based without a three month follow-up. The worse outcome during NH in our study was not accounted for by differences in measured patient characteristics, rates of or delays in recanalization therapy.

Strengths and limitations

One strength of the present study is the large sample size (n=35,261) with low number of missing data on primary outcomes (9.8%). We used key performance measures as well as functional outcome at 3 months as outcomes in a prospectively collected dataset. Furthermore, data collection was performed from 01/2014 up to 12/2019 resulting in up-to-date analyzes reflecting the current situation of real world stroke service provision.

Our study has some limitations: Apart from general limitations of registry based, retrospective studies we were unable to clarify why performance measures and outcomes are worse during NH and can only make assumptions. It is possible that unmeasured differences between OH and NH were missed in patients or settings, leading to residual confounding. We were not able to investigate if the improvement of DPT over time was associated with increased economic costs. As we do not know the exact staff levels of each participating center we were not able to calculate optimal staffing during NH. Also, our results may not be generalizable to countries with different organization of acute stroke care, different distribution of acute stroke patients (in our study most patients were admitted to a Stroke Center) and more limited availability of infrastructure and staff.

Summary/conclusions

The delivery of acute recanalization therapy at Swiss Stroke Centers and Stroke Units is moderately delayed during non-office hours. Patients admitted during NH have a worse functional outcome which is not explained by availability or delay of recanalization therapy. Recent evidence and recommendations for treatment of wake-up stroke have been quickly adopted over the past few years. Overall, our findings show that Stroke Centers and Stroke Units certified in accordance to European guidelines are capable of providing round-the-clock acute stroke care, which may inform the planning of service provision in other health care systems.

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Declaration of conflicting interests

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Informed consent

In accordance with national law, patients were informed about the use of their routinely collected data for research purposes. Patients who denied use of their data were excluded from the analysis.

Ethical approval

Ethical approval for this study was waived by the EKNZ (Ethikkommission Nordwest- und Zentralschweiz) because the study was classified as a Quality Assurance Study.

Guarantor

LHB

Contributorship

VLA designed/conceptualized the study, interpreted the data, and drafted the manuscript. PRW and SAS performed statistical analyzes, interpreted data, and revised the manuscript. LHB designed/conceptualized and initiated the study, supervised the study, collected data, interpreted the data, revised the manuscript, and is the Coordinator of the Swiss Stroke Registry. GMDM, HG, STE, MP, UF, TM and JK contributed to the conception and design of the study. KN, TK, MA, UF, MG, TM, PM, JK, EC, PM, CWC, MB, AvH, GK, JV, JW, ARL, SW, NP, SS, RS, FM, CBe, LS, SR, JN, CBo, MS, MLM, BR and GS contributed to drafting the text, preparing the figures, and the acquisition of data.

Trial registration

Not applicable.

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Supplemental material

Supplemental material for this article is available online.

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