Journal of Neurology (2019) 266:782–789
https://doi.org/10.1007/s00415-018-9079-1

NEUROLOGICAL UPDATE

Comparison of outcome in stroke patients admitted during working hours vs. off-hours; a single-center cohort study

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Received: 6 August 2018 / Revised: 25 September 2018 / Accepted: 26 September 2018 / Published online: 5 October 2018

Abstract

Introduction We aimed to disprove an in-hospital off-hour effect in stroke patients by adjusting for disease severity and poor prognostic findings on imaging.

Patients and methods Our study included 5378 patients from a single center prospective stroke registry of a large teaching hospital in the Netherlands, admitted between January 2003 and June 2015. Patients were categorized by admission time, off-hours (OH) or working hours (WH). The in-hospital mortality, 7-day mortality, unfavorable functional outcome (modified Rankin scale > 2) and discharge to home were analyzed. Results were adjusted for age, sex, stroke severity (NIHSS score) and unfavorable findings on imaging of the brain (midline shift and dense vessel sign).

Results Overall, 2796 patients (52%) were admitted during OH, which had a higher NIHSS score [3 (IQR 2–8) vs. 3 (IQR 2–6): $p < 0.01$] and had more often a dense vessel sign at admission (7.9% vs. 5.4%: $p < 0.01$). There was no difference in mortality between the OH-group and WH-group (6.2% vs. 6.0%; $p = 0.87$). The adjusted hazard ratio of in-hospital mortality during OH was 0.87 (95% CI: 0.70–1.08). Analysis of 7-day mortality showed similar results. Unadjusted, the OH-group had an unfavorable outcome [OR: 1.14 (95% CI: 1.02–1.27)] and could less frequently be discharged to home [OR: 1.16 (95% CI: 1.04–1.29)], which was no longer present after adjustment.

Discussion and conclusions The overall outcome of stroke patients admitted to a large Dutch teaching hospital is not influenced by time of admission. When studying OH effects, adjustment for disease severity and poor prognostic findings on imaging is crucial before drawing conclusions on staffing and material.

Keywords Stroke · Off-hours · Off-hour effect · Severity · In-hospital mortality

Introduction

Stroke is the second leading cause of death worldwide and the third largest contributor to disease burden [1]. Obviously, to limit stroke mortality and morbidity, it is important to maintain high quality of care 24 h a day.

Previous studies report differences in outcome of stroke patients associated with time of admission. A systematic review and meta-analysis of 21 studies in 2014 concluded that patients with acute ischemic stroke admitted during off-hours (OH) have higher short-term mortality and greater disability at discharge compared to those admitted during working hours (WH) [2]. This "OH effect" may be attributed to less (experienced) staff, less available diagnostic procedures, variations in the processes of care and decreased likelihood of delivering thrombolytic and intra-arterial therapy [2–4]. The OH effect was also found in patients suffering from several other diseases, such as myocardial infarction, pulmonary embolism, and ruptured abdominal aortic aneurysm [5, 6]. A recent international study analyzed 30-day in-hospital mortality in nearly 3 million admissions and has shown a "weekend effect" in multiple hospitals as well [7].

However, studies adjusted for stroke severity did not confirm an OH effect in stroke patients [8–16]. Patients admitted during OH may suffer from more severe strokes and therefore adjusting for stroke severity seems essential when investigating the existence of an OH effect [10, 17]. Only

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few studies report an OH effect with adjustment for patients' physical conditions [17–23].

In summary, a large number of studies with inconsistent findings have been performed to investigate an OH effect for stroke patients. Upgrading staff levels and diagnostic procedures during OH is expensive, and resources are limited. Therefore, more studies are necessary before implementing such costly changes. We aimed to investigate the existence of an OH effect on stroke outcome after admission to a large teaching hospital in the Netherlands with proper adjustment for stroke severity and poor prognostic findings on imaging.

Methods

Setting

In this retrospective cohort study, we analyzed all patients included in the Enschede Stroke Service, an ongoing patient-linked database of patients admitted to the stroke unit of a teaching hospital in Enschede, the Netherlands (Medisch Spectrum Twente). Our stroke unit has a capacity of 11 beds for approximately 800 stroke patients per year. Since September 2013, intra-arterial thrombectomy is performed in our center. Complete stroke care, including imaging, intravenous thrombolysis, and intra-arterial thrombectomy, is available around the clock. Stroke diagnostic and treatment protocols are identical during OH and WH including ECG and brain imaging on admission, at least 24-h of ECG monitoring and a routine swallowing test. During WH, the emergency service, the stroke unit and the general ward are occupied by three neurology residents, supervised by two neurologists. During OH, there is one neurology resident present who is responsible for all three departments, supervised by one neurologist on-call.

Finally, nurse staffing is reduced during OH. During weekdays at daytime, three nurses are at work (of which one nurse half a shift) instead during weekend at daytime when two nurses are. Both in weekends and weekdays, during the evening two nurses are at work (of which one nurse half a shift) and during the night one.

Study population and time of admission

We included all patients with ischemic stroke or intracerebral hemorrhage who were admitted to our hospital between January 2003 and June 2015. We excluded in-hospital stroke patients and patients who were transferred to or referred from other hospitals. Patients with a TIA who were completely recovered on admission were also excluded.

Patients were categorized in two groups by time of admission. We defined WH on weekdays between 08:30 h and 16:59 h, in line with the maximum occupation of the medical staff. Admissions during weekdays between 17:00 h and 8:29 h the next morning, Saturdays, Sundays, and national holidays, were defined as OH.

Outcome measures and study variables

The primary outcome measure was overall in-hospital mortality. Second, we analyzed mortality within 1 week of admission, unfavorable outcome at discharge and the proportion of patients who could not be discharged to their own home. Functional outcome was assessed by the modified Rankin scale (mRS score). Unfavorable functional outcome was defined as a mRS score > 2 [24].

All outcome measures were adjusted for age, sex, stroke severity and unfavorable findings on Computer Tomography (CT) of the brain on admission. Stroke severity was assessed by the NIH Stroke Scale (NIHSS) [25, 26]. Unfavorable findings on CT include the presence of a dense vessel sign and/or midline shift, as these CT findings are associated with increased stroke mortality [27, 28].

Moreover, the outcome measures were adjusted for possible confounders. Possible confounders include treatment (intravenous thrombolysis and/or treatment with intra-arterial thrombectomy) and baseline characteristics (smoking, overweight (Body Mass Index > 25), hyperlipidemia, hypertension, previous stroke, family history, atrial fibrillation, mRS score before admission, the number of patients who lived at home before admission). Adjustments were made if possible confounders were significantly different between the OH-group and WH-group ($p < 0.05$).

Statistical analysis

Statistical analysis was performed using a Student's *t* test or Mann–Whitney *U* test (if data were not normally distributed) for continuous variables and the Chi-square test for categorical variables. We compared in-hospital mortality between the OH-group and the WH-group, by means of Cox regression analysis. Second, we analyzed unfavorable functional outcome and the percentage of patients who were discharged to home, using a multivariable logistic regression analysis. Statistical analysis was performed with SPSS 17.0 and 20.0 edition.

Results

From January 2003 to July 2015, 6210 patients were admitted to our stroke unit. As shown in Fig. 1, 5378 patients met our inclusion criteria, of which 2796 patients (52%) were included in the OH-group and 2582 patients (48%) in the WH-group. In 507 patients (9.4%), intracerebral hemorrhage

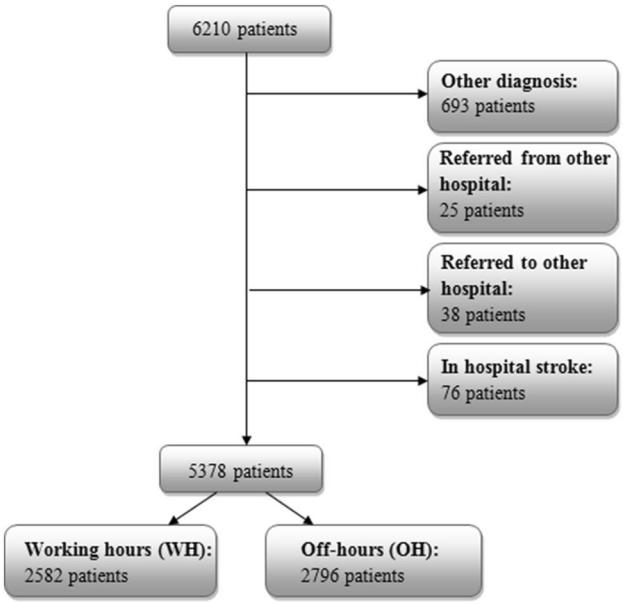

Fig. 1 Flowchart of study exclusion criteria and group size

was diagnosed, which was present more often in the OH-group than in the WH-group (10.3% vs. 8.4%; $p=0.02$).

During OH, patients were slightly younger and treatment with intravenous rtPA and intra-arterial thrombectomy was performed more frequently (Table 1).

Furthermore, in the OH-group, the NIHSS score on admission was significantly higher and a dense vessel sign was observed more often on the admission CT scan (Table 2).

Overall, the in-hospital mortality rate was 6.1% ($n=328$). There was a non-significant difference between the two groups (OH-group $n=172$ (6.2%) vs. WH-group $n=156$ (6.0%); $p=0.87$). Adjusted for age, sex, intravenous thrombolysis, intra-arterial thrombectomy, NIHSS score and poor prognostic CT findings, the hazard ratio of in-hospital mortality due to OH admission was 0.89 (95% CI: 0.71–1.10). Analysis of 7d mortality showed the same non-significant results (Table 3).

Figure 2 shows the percentages of mRS score at discharge of the OH-group and WH-group in more detail. Unadjusted, more patients in the OH-group had unfavorable outcome compared to patients in the WH-group. After adjustment for

Table 1 Baseline characteristics

	OH-group ($n=2796$)	WH-group ($n=2582$)	p value
Age, mean (SD)	70.1 years (±13.3)	70.8 years (±13.0)	0.03*
Women	1333 (47.7%)	1251 (48.5%)	0.57
Smoking	806 (28.8%)	696 (27.0%)	0.13
Overweight	1073 (38.5%)	965 (37.4%)	0.44
Hyperlipidaemia	2109 (75.4%)	1952 (75.6%)	0.88
Hypertension	1849 (66.1%)	1713 (66.3%)	0.87
Diabetes	678 (24.2%)	624 (24.2%)	0.94
Positive family history	580 (20.7%)	531 (20.6%)	0.87
Atrial fibrillation	619 (22.1%)	533 (20.6%)	0.18
Previous stroke	667 (23.9%)	628 (24.3%)	0.69
mRS score before admission[a]	0 (0–1)	0 (0–1)	0.46
Patients living at home before admission	2608 (92.8%)	2397 (93.3%)	0.53
Intravenous thrombolysis with rtPA[b]	370 (14.8%)	240 (10.2%)	<0.01*
Intra-arterial thrombectomy[b]	22 (0.9%)	7 (0.3%)	<0.01*

*Significantly different

[a]Median (IQR)

[b]These percentages are solely based on patients with an ischemic stroke (OH: $n=2507$; WH: $n=2364$)

Table 2 Stroke severity and unfavorable CT findings at baseline

	OH-group ($n=2796$)	WH-group ($n=2582$)	p value
Midline shift on CT	227 (8.1%)	191 (7.4%)	0.32
Dense vessel sign[b]	197 (7.9%)	128 (5.4%)	<0.01*
NIHSS score on admission[a]	3 (2–8)	3 (2–6)	<0.01*

*Significantly different

[a]Median (IQR)

[b]These percentages are solely based on patients with an ischemic stroke (OH: $n=2507$; WH: $n=2364$)

Table 3 Unadjusted and adjusted outcome measures in OH-group compared to WH-group (total population)

	Hazard ratio/odd's ratio
In-hospital mortality	
Unadjusted	HR: 1.00 (95% CI: 0.81–1.24)
Adjusted	HR: 0.87 (95% CI: 0.70–1.08)
7d mortality	
Unadjusted	HR: 1.13 (95% CI: 0.87–1.45)
Adjusted	HR: 0.94 (95% CI: 0.73–1.22)
Unfavorable outcome	
Unadjusted	OR: 1.14 (95% CI: 1.02–1.27)*
Adjusted	OR: 1.04 (95% CI: 0.90–1.20)
Not discharged to home	
Unadjusted	OR: 1.16 (95% CI: 1.04–1.29)*
Adjusted	OR: 1.06 (95% CI: 0.92–1.22)

*Significantly different

age, sex, intravenous thrombolysis, intra-arterial trombectomy, stroke severity and poor prognostic CT findings, admission during OH was not associated anymore with unfavorable functional outcome (Table 3). This is in line with the results of discharge to home. Unadjusted, more patients admitted during OH could not be discharged to home, but this difference disappeared after adjustment (Table 3).

Finally, Table 4 shows the results for ischemic stroke patients and patients with intracerebral hemorrhage, separately. Again no significant differences were observed after adjustment.

Discussion

In this study, admission during OH was not associated with higher in-hospital mortality. Analysis for subgroups (ischemic stroke and intracerebral hemorrhage) and 7-day

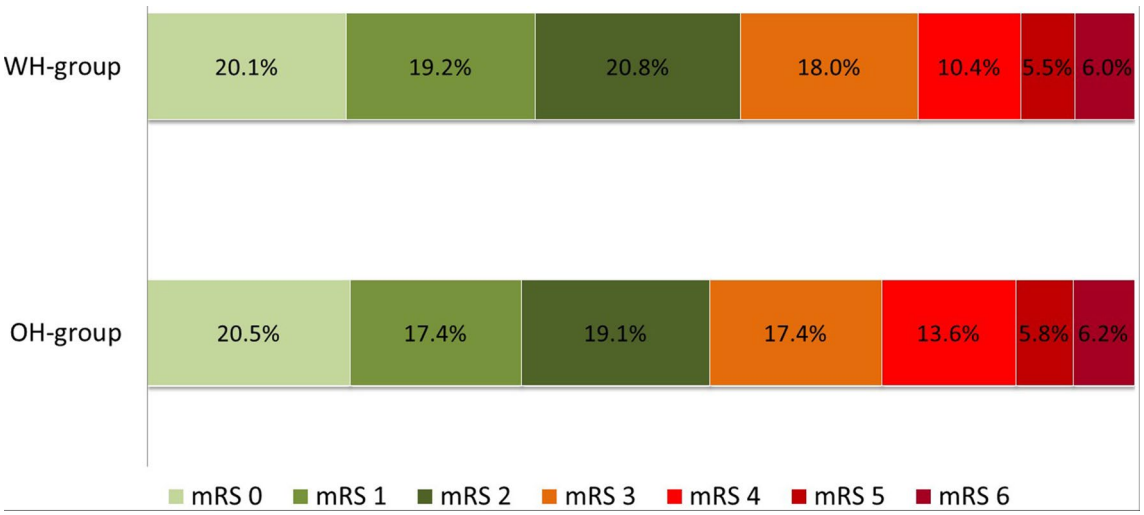

Fig. 2 Functional outcome: mRS score at discharge of the OH-group and WH-group

Table 4 Unadjusted and adjusted outcome measures in OH-group compared to WH-group in ischemic and haemorrhagic stroke patients separately

	Ischemic stroke	Intracerebral hemorrhage
In-hospital mortality		
Unadjusted	HR: 0.89 (95% CI: 0.68–1.18)	HR: 1.02 (95% CI: 0.72–1.44)
Adjusted	HR: 0.81 (95% CI: 0.61–1.07)	HR: 0.93 (95% CI: 0.65–1.32)
7d mortality		
Unadjusted	HR: 1.02 (95% CI: 0.73–1.43)	HR: 1.06 (95% CI: 0.72–1.57)
Adjusted	HR: 0.86 (95% CI: 0.61–1.22)	HR: 0.99 (95% CI: 0.67–1.47)
Unfavorable outcome		
Unadjusted	OR: 1.12 (95% CI: 0.99–1.25)	OR: 1.07 (95% CI: 0.71–1.63)
Adjusted	OR: 1.03 (95% CI: 0.89–1.20)	OR: 0.95 (95% CI: 0.56–1.60)
Not discharged to home		
Unadjusted	OR: 1.12 (95% CI: 1.00-1.26)	OR: 1.23 (95% CI: 0.81–1.87)
Adjusted	OR: 1.04 (95% CI: 0.89–1.20)	OR: 1.22 (95% CI: 0.73–2.04)

mortality showed similar results. A higher percentage of patients admitted during OH had unfavorable functional outcome and a lower chance of discharge to home compared to patients admitted during WH. However, after adjustment for stroke severity and for poor prognostic findings on imaging, these differences were no longer significant. This confirms that possible OH effect is likely due to these prognostic factors instead of time of admission.

Our overall in-hospital mortality percentage is comparable with or even more favorable than those reported in other studies [9, 15, 16]. Our data confirm that stroke patients admitted during OH have more severe strokes and more frequently have signs on brain imaging, indicating larger infarct zones and less favorable prognosis [10, 16, 17, 29]. Furthermore, the differences between non-adjusted and adjusted outcomes in our and other studies underscore the need for proper adjustment for these factors [10, 11, 14, 16]. We believe that our results are more reliable than studies which were not able to adjust for stroke severity [3, 4, 30–34].

Nevertheless, some studies found a worse outcome in patients admitted during OH even despite adjustment for patients´ physical conditions or stroke severity [17–23]. Some of these studies did not use the international accepted NIHSS for measurement of stroke severity [17, 19, 20, 22, 23]. Besides, some of these studies compared admissions during weekdays vs. the weekend [17, 18, 20]. It is more plausible that differences in patients' characteristics, available (experienced) staff and availability of diagnostic and therapeutic procedures exist during all OH and not only during the weekend. For example, a recent study of Bray et al. [21] shows no difference in 30-day survival after adjustment for stroke severity between weekdays and weekends. However, they found lower survival odds in patients admitted during weekdays after 8 pm compared with admission during weekdays before 8 pm [OR 0.90 (95% CI: 0.82–0.99)]. Therefore, in our opinion, comparing outcome between WH and OH is more accurate. Although Bray et al., found an OH-hour effect, most studies adjusting for stroke severity and comparing OH vs. WH found no association between time of admission and mortality in line with our results [10, 11, 13–15, 35].

Besides mortality, previous studies also investigated the influence of the time of admission on functional outcome and discharge location. Like our results, Jauss et al. [10] found that ischemic stroke patients admitted during OH have unfavorable functional outcome which was no longer present after adjustment for stroke severity. Streifler et al. [16] showed that the greater proportion of patients with intracerebral hemorrhage during OH presentation in their cohort was responsible for the less favorable functional outcome. After adjustment for several factors including stroke type, the relative odds for poor outcome were no longer significant. In our cohort, patients with an intracerebral hemorrhage were also overrepresented in the OH-group and had less favorable outcome compared to patients admitted during WH. However, we found no differences in outcome between OH and WH in the subgroup analysis based on event type. Other studies did not found a greater proportion of poor functional outcome for stroke patients admitted during OH, even without adjustment for stroke severity [8, 9, 12, 13, 15]. All of these studies were performed in specialized stroke centers.

Two Japanese studies found contrasting results regarding functional outcome. Nakajima et al. found that admission during OH was associated with unfavorable outcome at 3 months in patients with ischemic stroke who had to wait more than 48 h until the next working day [36]. However, we consider this long-term outcome less likely to reflect a direct effect of time of admission. Hasegawa et al. [18] showed that admission of stroke patients on a weekday was a significant positive prognostic factor for favorable outcome (mRS 0–1). However, this study population is not representative for current stroke care in the Western world since intravenous thrombolytic therapy was not yet approved in Japan.

In line with most previous studies, we preferred to categorize the outcome of stroke patients in favorable and unfavorable outcome instead of measuring the change in mRS score before and after hospital stay. Moreover, the mRS score on admission in our cohort did not differ between WH and OH (Table 1).

Two studies found no significant difference in discharge destination when comparing weekday and weekend admission of ischemic stroke and all stroke patients, respectively, even without adjustment for stroke severity [8, 9, 37]. In contrast, Saposnik et al. concluded that stroke patients admitted during weekends were less likely to be discharged home, but they did not adjust for stroke severity [3].

Besides mortality, functional outcome and discharge location, the presence of complications probably also represents the quality of care in stroke patients. In our cohort, subanalysis showed no difference in the frequency of complications between the two groups (results not shown) and a separate analysis to adjust our results for these complications did not change our results.

There are several potential explanations that the time of admission does not independently influence the outcome in stroke patients. Patients with mild strokes are more likely to wait until the next morning or after the weekend to seek medical help compared to patients with severe strokes [17, 20, 38]. In general, many patients are still unaware of the benefits of fast diagnosis and treatment. We consider this as the main reason why patients admitted during OH have more severe strokes compared to patients admitted during WH. It underscores the necessity to adjust for stroke severity and for unfavorable finding on imaging before drawing conclusions on staffing and nursing.

It is possible that there was no OH effect in our stroke population since our hospital has a well facilitated stroke

unit. McKinney et al. [31] found higher 90-day mortality in stroke patients admitted during the weekend in all New Jersey hospitals together, but not in the comprehensive stroke centers separately. Other authors, who did not found an OH effect, also attributed these results to high quality of care in comprehensive stroke centers [8, 9, 15].

Furthermore, the fact that our hospital is a teaching hospital could partly explain the absence of an OH effect. It is suggested that in general the overall quality of care in teaching hospitals is better [39]. Two studies found a weekend effect for ischemic stroke patients admitted to non-teaching hospitals and no effect in patients admitted to teaching hospitals [3, 40].

Another potential explanation for disproving an OH effect in our population is the international difference in the organization and quality of stroke care. Stroke care in The Netherlands is thought to be of high quality, in particular for the acutely admitted patients [41]. One of the reasons is the well-facilitated infrastructure and nearly always a hospital with stroke care facilities within close range. Studies which found an OH or weekend effect in the Netherlands used administrative datasets and were not able to adjust for disease severity [7, 34].

Finally, instead of a negative OH effect, there might even be a positive effect of admission during off hours. Curtze et al. [29] analyzed the outcome of ischemic stroke patients treated with intravenous thrombolysis in the Helsinki University Central Hospital and even found better functional outcome in patients admitted during OH, but no difference in outcome when comparing weekend vs. weekday admission. Furthermore, some studies show shorter delay of brain imaging during OH, which seems to be in contrast with the hypothesis that diagnostic procedures are less available during OH [16, 42, 43]. The chance of receiving intravenous thrombolysis, in line with our results, seems to be the same or even higher during OH [10, 14, 31, 37, 44]. A possible explanation is that OH cover almost 75% of all hours of a week, but only about 50% of stroke patients arrive in the hospital during these hours. Thus, although staff is reduced, the health workers seem to have more time for the patient and there are fewer patients at the same time in need of imaging techniques or other diagnostic tests. Moreover, Bodenant et al. found higher case fatality rates for patients treated with intravenous thrombolysis during WH [45].

The main strengths of this study are the large number of patients, the detailed clinical data that are collected prospectively and the long period of included patients. To disprove an OH effect across the 12 years of study, we performed a subanalysis by dividing the total research group in three small groups (admission 2003–2007; 2008–2011 and 2011–June 2015). Again, no OH effect was proven (results not shown). The prospectively collected data made it possible to analyze and adjust for many different variables, in contrast to studies which used administrative databases [3–6, 22, 30, 31, 33, 34, 37, 46, 47]. Administrative databases do not include precise clinical information on severity and also have a margin of error [48, 49]. To our knowledge, only one other study adjusted for indicators of poor prognosis on brain imaging [29].

Our study also has some limitations. As it is a single center cohort study, we have to be careful to generalize our results to other clinical settings in the Netherlands or to hospitals abroad. Another limitation is the availability of short-term functional outcome only.

Conclusion

The overall outcome of stroke patients admitted to a Dutch teaching hospital, adjusted for stroke severity and for poor prognostic factors on imaging, is not influenced by time of admission. When studying OH effects, a proper adjustment for these confounders is crucial before drawing conclusions on staffing and material. We emphasize that our results are applicable only to comparable teaching hospitals and stroke centers.

Compliance with ethical standards

Conflicts of interest The authors declare that there is no conflict of interest. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical standard Neither an ethical approval nor an informed consent was sought for this article because this study is a retrospective cohort study of anonymously collected data. This study was completed in accordance with the Helsinki Declaration as revised in 2013.

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