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Late Night Activity Regarding Stroke Codes: (LuNAR strokes)

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Abstract

Background—There is diurnal variation for cardiac arrest and sudden cardiac death. Stroke may show a similar pattern. We assessed whether strokes presenting during a particular time of day or night are more likely of vascular etiology.

Aim—To compare emergency department stroke codes arriving between 10 pm and 8 am (LuNAR strokes) vs. others (n-LuNAR strokes). The purpose was to determine if late night strokes are more likely to be true strokes or warrant acute tissue plasminogen activator evaluations.

Methods—We reviewed prospectively collected cases in the University of California, San Diego Stroke Team database gathered over a four-year period. Stroke codes at six emergency departments were classified based on arrival time. Those arriving between 10 pm and 8 am were classified as LuNAR stroke codes, the remainder were classified as 'n-LuNAR '. Patients were further classified as intracerebral hemorrhage, acute ischemic stroke not receiving tissue plasminogen activator, acute ischemic stroke receiving tissue plasminogen activator, transient ischemic attack, and non-stroke. Categorical outcomes were compared using Fisher's Exact test. Continuous outcomes were compared using Wilcoxon Rank-sum test.

Results—A total of 1607 patients were included in our study, of which, 299 (19%) were LuNAR code strokes. The overall median NIHSS was five, higher in the LuNAR group (n-LuNAR 5, LuNAR 7; p=0.022). There was no overall differences in patient diagnoses between LuNAR and n-LuNAR strokes (p=0.169) or diagnosis of acute ischemic stroke receiving tissue plasminogen activator (n-LuNAR191 (14.6%), LuNAR 42 (14.0%); p=0.86). Mean arrival to CT scan time was longer during LuNAR hours (n-LuNAR 54.9±76.3 mins, LuNAR 62.5±87.7 mins; p=0.027). There was no significant difference in 90 day mortality (n-LuNAR 15.0%, LuNAR 13.2%; p=0.45)

Conclusions—Our stroke center experience showed no difference in diagnosis of acute ischemic stroke between day and night stroke codes. This similarity was further supported in similar rates of tissue plasminogen activator administration. Late night strokes may warrant a more rapid stroke specialist evaluation due to the longer time elapsed from symptom onset and the longer time to CT scan.

Keywords

acute stroke therapy; cerebral infarction; epidemiology; ischaemic stroke; rtPA; stroke teams; thrombolysis; treatment

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Introduction

Stroke is the third leading cause of death worldwide and is the leading cause of long-term disability in the United States (1–2). Following Food and Drug Administration (FDA) approval of tissue plasminogen activator (t-PA) in 1996, acute ischemic stroke has been recognized as a medical emergency similar to acute myocardial infarction. Since t-PA has been approved, only 3–8.5% of ischemic stroke patients receive the medication (3). It is well established that myocardial infarction follows a circadian rhythm, with a higher risk between 6 am and noon (4). Although the exact reason remains unclear, this may be due to physical activity, blood pressure variation, plasma cortisol, and catecholamine release.

The evidence for diurnal variation in stroke has not been fully clarified. A meta-analysis of 31 publications reporting the circadian timing of 11 816 strokes, reported that there was a 49% increase in stroke between 6 am and noon. Marsh *et al* (5) found similar results in all subgroups of ischemic stroke. Further, the time period with the lowest risk for stroke was found to be between midnight and 6 am (6). Multiple studies have demonstrated that approximately one out of five strokes occur at night (5,7,8). Patients who wake up with stroke symptoms are usually not candidates for thrombolytics because of the unclear time of onset. Training professionals to obtain a thorough history may increase the likelihood of treatment by refining the suspected time of onset, as it is common to have intermittent periods of waking up at night for various reasons, thus helping to clarify the time the patient was last known to be without deficit. Marsh *et al* (5) demonstrated that approximately 30% of patients had the onset of ischemic stroke within one-hour of awakening.

A recent Canadian study found that stroke patients admitted on weekends had higher mortality rates than those admitted during the weekday (9). A 24/7 acute stroke team in a primary stroke center may likely ameliorate this problem, possibly due to the availability of stroke team specialty practitioners (10). With the availability of 24/7 acute stroke teams, more patients who present with ischemic strokes during late night hours may be able to receive acute thrombolytic therapy if they are actual stroke presentations.

Hypothesis

Though there may be other benefits of acute stroke evaluations unrelated to t-PA administrations; there is a general, but untested hypothesis that late night stroke codes may not be true acute strokes or will not qualify for thrombolytic interventions due to significant time since symptom onset. If this hypothesis holds true, it may not be necessary to have late night stroke coverage. If this is not the case, ensuring there is a 24/7 acute stroke code team may be fundamental to treating more stroke patients. In an effort to determine if strokes that occur late at night are more or less likely to be candidates for thrombolytic therapy, we performed a cohort study to explore this issue at one tertiary care stroke center and surrounding covered hospitals.

Methods

The University of California, San Diego (UCSD) Stroke Team consists of two board certified vascular neurologists and two vascular neurology fellows. We provide 24/7 vascular neurology trained specialist coverage to stroke codes at six different hospitals in the San Diego area. Of the six hospitals, two are academic facilities, one is a Veteran's hospital and three are community/private hospitals. Five out of six hospitals are certified by the Joint Commission (TJC) (11). This study is based on 1607 patients designated stroke codes from six emergency departments (ED) that were consecutively included in the prospective UCSD Specialized Programs of Translational Research in Acute Stroke (SPOTRIAS) database from June 2004 to August 2008. The UCSD SPOTRIAS database is an NIH funded

computerized, prospective, observational database with demographic and outcome stroke data from patients seen at the aforementioned hospital EDs. The patients were classified based on their ED arrival time. Patients arriving between the hours of 10 pm and 8 am were arbitrarily designated as LuNAR stroke codes and patients admitted between the hours of 8 am and 10 pm were considered n-LuNAR stroke codes.

The patients were further categorized into the following diagnosis groups:

- intracerebral hemorrhage
- acute ischemic stroke not receiving rt-PA (AIS − rt-PA)
- acute ischemic stroke receiving rt-PA (AIS + rt-PA)
- transient ischemic attack (TIA), and
- other (Table 3).

For both the ‘LuNAR ‘and n-LuNAR stroke code groups, we compared the in-hospital mortality, 90 day mRS (0–2 vs. 3–6) and 90 day mortality (mRS=6). A mRS of 0–2 indicated a favorable outcome and 3–6 was a poor outcome. We evaluated 90 day outcome data and mortality on only the patients that were consented. Patient demographics, NIHSS scores, admission glucose levels and treatment times were examined.

Comparisons between the LuNAR and n-LuNAR groups were made using the Wilcoxon Rank-sum test for continuous variables and the Fisher’s Exact test for categorical variables. In-hospital mortality was compared between arrival groups using a Fisher’s Exact test. Multivariable logistic regression was performed to determine the association between binary outcome (day 90 mRS of 0–2 vs. 3–6, and 90 day mortality) and arrival groups, adjusting for the following confounders:

- age
- admission NIHSS scores
- admission glucose, and
- use of intravenous (IV) rt-PA.

Results were reported with odds ratio (OR) and 95% confidence intervals. Treatment times were compared between arrival groups using Wilcoxon Rank-sum test. This study has been Institutional Review Board (IRB) approved at all of the participating facilities.

Results

Of 1607 patients, 299 (19%) were categorized as LuNAR stroke codes. The overall median age was 68 years (range 18–99). The majority of patients identified themselves as white (79.1%) and about half of them were men (51.5%). Patients who presented as LuNAR strokes had a significantly higher median NIHSS score (5 n-LuNAR vs. 7 LuNAR; p=0.022). The mean admission glucose values were similar for n-LuNAR and LuNAR strokes (144±78 n-LuNAR vs. 135±66 LuNAR; p=0.092). The frequency of diagnosis of acute ischemic stroke during n-LuNAR and LuNAR hours was similar (46% n-LuNAR vs. 52% LuNAR, p=0.073). There was no significant difference in IV t-PA treatment rates during n-LuNAR and LuNAR stroke code hours overall (191 (14.6%) n-LuNAR vs. 42 (14.0%) LuNAR; p=0.86). The subset of patients with an acute ischemic stroke diagnosis presenting during LuNAR hours were less likely to receive IV or intra-arterial (IA) thrombolytic therapy compared to n-LuNAR hours (31.3% n-LuNAR vs. 26.8% LuNAR: p=0.29), although this difference was not statistically significant.

Treatment times during both time periods were similar, with the exception of arrival to CT scan, which was slightly longer during LuNAR hours (54.9min±76.3 n-LuNAR vs. 62.5min ±87.7 LuNAR; p=0.027). There were no significant differences in times of arrival to lab evaluation (62.4min±67.3 n-LuNAR vs. 68.8min±78.5 LuNAR; p=0.403) and bolus administration of rt-PA between groups (81.8min±42.8 n-LuNAR vs. 81.2min±27.9 LuNAR; p=0.379).

The mean time between onset of symptoms and arrival was 194 mins during n-LuNAR hours and 234 mins during LuNAR hours (194min±395 n-LuNAR vs. 234min±319 LuNAR; p<0.0001). There were no significant differences between onset of stroke symptoms to bolus administration of rt-PA between groups (146min±73 n-LuNAR vs. 163min±118 LuNAR; p=0.202).

There were no significant differences between arrival to treatment decisions between n-LuNAR and LuNAR stroke codes (69.1min±62.7 n-LuNAR vs. 74.9min±90.8 LuNAR; p=0.365). There were no statistically significant differences in hospital mortality rates (OR=0.91; 95% C.I. (0.52, 1.51); p=0.804), 90 day functional outcome (adjusted OR=0.52; 95% C.I. (0.25, 1.09); p=0.083) or mortality at 90 days (adjusted OR=0.70; 95% C.I. (0.28, 1.77); p=0.45), in either group.

Discussion

Patients presenting during LuNAR hours as ‘stroke code’ activations had a high rate of acute ischemic stroke diagnoses even in these late night hours. Not only do late night stroke activations represent true acute ischemic strokes, but it is possible that these cases require the most rapid of stroke specialist responses given the longer time elapsed from symptom onset to ED arrival and the longer time to CT scan. Interestingly, we also found that there were similar rates of t-PA in those arriving during n-LuNAR hours. Patients with the diagnosis of acute ischemic stroke arriving during LuNAR hours were less likely to receive IV or IA t-PA. This may be due to the patients waking up with the deficit and being out of the thrombolytic window. These results emphasize the need for stroke code activation on all suspected stroke codes, irrespective of time, to increase potential thrombolytic treatments and appropriately manage acute strokes. This also supports the need for cerebrovascular specialists to be available in the late night (LuNAR) hours. The mean time between the onset of stroke symptoms and arrival to the ED was significantly shorter during n-LuNAR hours compared to LuNAR hours. This may be due to patients being more isolated with limited access to others during late night hours.

When looking at the acute ischemic stroke subset diagnosis during LuNAR and n-LuNAR hours, the patients arriving during LuNAR hours were less likely to receive thrombolytics, perhaps due to a higher percentage of patients having unknown times of onset or awakening with the deficit and, therefore, not qualifying for t-PA treatment. Similar times-to-decisions and patient outcomes found in these groups of patients support the belief that the presence of a 24/7 acute stroke team can maintain consistency any time of the day, possibly due to established care pathways even during LuNAR hours. In our assessment, patients admitted for acute ischemic stroke during LuNAR hours, had more severe strokes than those admitted during n-LuNAR hours. Approximately 1/3 of our LuNAR and n-LuNAR stroke codes resulted in a diagnosis of ‘non-stroke’. Treatment times did not differ between LuNAR and n-LuNAR strokes, with the exception a slightly longer time to CT at night. This could be due to limited hospital resources during the night.

Our analysis found no differences in hospital mortality rates, 90 day functional outcome, or mortality at 90 days in either group. Contrary to our findings, a recent study by Reeves *et al*,

evaluating in-hospital mortality during the hours between 6 pm and 7 am for ischemic and hemorrhagic strokes found and increased risk of in hospital mortality (12). This discrepancy may be due to our small sample size.

Our results suggest that maintenance and resource support for a 24/7 stroke team are integral to a successful stroke treatment program. These results are supported by the similar rates of acute ischemic stroke for these patients that arrive to the ED during LuNAR hours and n-LuNAR hours. The results of the LuNAR study could be due to the presence of a 24/7 stroke team, and do require confirmation in other stroke centers and other cohorts. A prospective comparison of a center with a comprehensive stroke program, to one without such 24/7 coverage could determine conclusively if this holds true. Based on this large cohort, this study demonstrates that, although the actual incidence of stroke codes was less during LuNAR hours, the rate of treatment with tissue plasminogen activator was the same during both LuNAR and n-LuNAR hours. Late night stroke activations are as likely to be an acute ischemic stroke as during daytime hours. With the longer times to CT at night, it is imperative that we maintain the urgency for rapid evaluation and treatment. LuNAR stroke codes are of equal importance and programmatic emphasis and stroke center certifications should ensure care of patients irrespective of time of day or night.

Limitations

The limitations of our study are that not all ‘stroke code’ patients received a 90 day evaluation and therefore bias may have been introduced into our outcome analysis. We do, however, show 100% follow up on hospital discharge. Further, our design is limited by its retrospective analysis even though it was from data collected prospectively on this cohort.

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Table 1

Baseline characteristics of LuNAR and n-LuNAR groups

	LuNAR	n-LuNAR	P value
	(N=299)	**(N=1308)**	
Age – years (Mean±sd)	64.9±17.9	67.1±16	0.087
Men (%)	55.2	50.7	0.178
Median NIHSS	7	5	0.022
Glucose (Mean±sd)	143.5±77.6	134.8±66.2	0.092
Hispanic (%)	14.7	14.1	0.784

Table 2

Treatment times (mins)

	LuNAR	n-LuNAR	P value
Arrival to CT scan	62±88	55±76	0.027
Arrival to lab evaluation	69±78	62±67	0.403
Arrival to treatment decision	75±91	69±63	0.365
Arrival to bolus	81±28	82±43	0.379
Onset to arrival	234±319	194±395	<0.0001
Onset to bolus	163±118	146±73	0.202

Table 3

Patient Diagnosis

	LuNAR (N=299)	n-LuNAR (N=1308)	P
Patient Diagnoses			0.169
ICH	20 (7%)	111 (9%)	
AIS − t-PA	115 (39%)	420 (32%)	
AIS + t-PA	42 (14%)	191(15%)	
TIA	23 (8%)	144 (11%)	
Other	99 (33%)	442 (34%)	

Table 4

Reasons for exclusion from tPA in AIS patients

	Day	LuNAR	Total
Over three-hours	242	81	323
Too mild	134	28	162
Rapid improving	44	7	51
Pt/family refused	6	4	10
Current hemorrhage	10	2	12
Anticoagulated	27	4	31
Blood pressure	10	1	11
Blood glucose	0	1	1
Mimic	8	2	10
Other	47	12	59

Table 5

Outcomes

	LuNAR (N=76)*	n-LuNAR (N=428)*	P value§
Day 90 mortality (mRS 6)	10 (13%)	64 (15%)	0.45†
Day 90 mRS			
0–2	48 (63%)	244 (57%)	0.083†
3–6	28 (37%)	184 (43%)	
	(N=299)	(N=1308)	
In Hospital Mortality	20 (7%)	96 (7%)	0.804

*Fewer patients have 90-day follow up information in the database.

§P-values unadjusted for multiple comparisons

†P-value from multivariable logistic regression analysis adjusted for age, NIHSS scores on admission, admission glucose, use of IV rt-PA