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Stroke Severity Affects Timing: Time From Stroke Code Activation to Initial Imaging is Longer in Patients With Milder Strokes.

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Stroke severity affects timing – time from stroke code activation to initial imaging is longer in patients with milder strokes

Milder strokes have longer code-to-imaging times

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ABSTRACT

Optimizing the time it takes to get a potential stroke patient to imaging is essential in a rapid stroke response. At our hospital, door-to-imaging time is comprised of two time periods: the time before a stroke is recognized, followed by the period after the stroke code is called during which the stroke team assesses and brings the patient to the CT scanner. To control for delays due to triage, we isolated the time period after a potential stroke has been recognized, as few studies have examined the biases of stroke code responders. This “code-to-imaging time” encompassed the time from stroke code activation to initial imaging, and we hypothesized that perception of stroke severity would affect how quickly stroke code responders act. In consecutively admitted ischemic stroke patients at The Mount Sinai Hospital emergency department, we tested associations between National Institutes of Health Stroke Scale scores, continuously and at different cutoffs, and code-to-imaging time using spline regression, t-tests for univariate analysis, and multivariable linear regression adjusting for age, sex, and race/ethnicity. In our study population, mean code-to-imaging time was 26 minutes, and mean presentation National Institutes of Health Stroke Scale score was 8. In univariate and multivariate analyses comparing code-to-imaging time between mild and severe strokes, stroke scale scores less than 4 were associated with longer response times. Milder strokes are associated with a longer code-to-imaging time with a threshold effect at a National Institutes of Health Stroke Scale score of 4.

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Introduction

Rapid brain imaging is essential when evaluating patients with suspected acute ischemic stroke in order to determine eligibility for treatment with intravenous alteplase (tPA) and endovascular thrombectomy. Guidelines recommend door-to-imaging time targets of < 25 minutes as delays result in longer door-to-needle times[1]. Mild strokes have longer delays, possibly due to poor symptom recognition by emergency department medical providers [2]. Analysis of the national "Get With The Guidelines–Stroke" database has shown that < 50% of tPA-eligible patients in the United States have door-to-imaging times of < 25 minutes, and continual efforts at process improvements are needed[3]. Some of the factors affecting door-to-imaging time are long emergency department (ED) registration times, incorrect triage diagnosis, and delayed stroke team activation[4]. The latter two factors involve improved stroke recognition during triage, and the ED nurses at The Mount Sinai Hospital (MSH) receive education on mild stroke symptoms to help address this. In the search for other ways to obtain timely imaging in patients with potential strokes, we wondered if there were issues after a stroke code had been activated that could also be slowing down the time to imaging. Thus rather than focusing on door-to-imaging time, potential triage delays were eliminated by looking at the time it takes to obtain brain imaging once a stroke code has been activated, i.e. "stroke code-to-imaging time" (CIT). We hypothesized that inherent responder biases based on first impressions of stroke severity may affect CIT, and therefore patients with lower National Institutes of Health Stroke Scale scores (NIHSS) would have longer CITs than those with higher NIHSS.

Methods

MSH is a 1,171-bed, comprehensive stroke center; neurology residents and stroke fellows are the first responders to stroke codes. Once a potential stroke is recognized by the primary team (in our study, the emergency department), a stroke code is activated for all suspected stroke patients presenting within 12 hours of time last known well (LKW). After stroke code activation, each member of the stroke team has pre-specified tasks which are performed in parallel: the emergency department physician enters the imaging order and assesses for medical stability for transport to CT scanner; nursing staff obtain intravenous access and blood for glucose testing; the patient care technician places a portable monitor; the neurologist obtains a targeted history and NIHSS and then helps move the patient to the CT scanner.

Out of 3409 patients in the Mount Sinai Hospital "Get With The Guidelines-Stroke" database from 2010-2015, 1865 were discharged with a diagnosis of ischemic stroke, of which 866 (46.4%) had stroke code activations in the ED. We eliminated patients with CT times occurring prior to stroke code activation (n=211) or with a LKW >12h from time of stroke code activation (n=302). The main cohort consisted of 353 patients with LKW <12h from stroke code activation. A secondary analysis was performed for patients who presented within the tPA window with LKW<4.5 hours (n=241). Code to imaging time (CIT), the primary outcome, was defined as the time between stroke code activation and CT scan initiation. Covariates included age, sex, and race/ethnicity. The main predictor assessed was the NIHSS, tested continuously and at six different dichotomous cutoffs (1-6).

All analyses were performed using SAS v9.4 (Cary, NC). Spline regression analysis was performed to explore trends. For univariate analyses, we used t-tests to compare CIT between mild and severe strokes, defined by NIHSS cutoffs ranging from 1-6, with both the main cohort and < 4.5h groups. Multivariable linear regression was performed in both groups, adjusting for age, sex, and race/ethnicity.

Results

The main cohort was predominantly elderly (70.9 years), female (58.4%) and evenly divided among race/ethnicity groups *(Table 1)*. Mean presentation NIHSS was 8, and more than 50% had an NIHSS ≤ 6 on presentation. LKW to code activation was on average 3.8 hours, and mean stroke code to imaging time (CIT) was 26 minutes. Spline regression suggested a threshold effect around an NIHSS of 4 on the outcome of CIT *(Figure).* NIHSS analyzed as a continuous variable was not significantly associated with delays in CIT. However, univariate analyses comparing CIT between low and high stroke scale groups showed that patients with higher NIHSS had a significantly shorter CIT (7.3 vs.16.7 minutes) at NIHSS cutoffs of 1-4 *(Table 2)*. Although CIT was still higher in the mild compared to severe stroke groups defined at NIHSS cutoffs of 5 and 6, the differences were not significant. These findings remained after adjustment for age, sex, and race/ethnicity.

The LKW < 4.5h subgroup comprised 68.3% of the main cohort and was demographically similar. Mean presentation NIHSS was 8 and greater than 50% presented with NIHSS<6 *(Table 1)*. In this group, the difference in mean CIT (5.9-19.1 minutes) was significant for all NIHSS cutoffs tested (1-6), including after adjustment for age, sex and race/ethnicity *(Table 2)*.

Discussion

In the MSH comprehensive stroke program, we found that mild strokes were associated with significantly longer stroke-code-to-imaging times (CITs), with a threshold effect at NIHSS 4; this effect remained after controlling for age, sex, and race/ethnicity. During stroke codes for patients presenting with an NIHSS < 4, it took 7.3 to 16.7 minutes longer to obtain brain imaging compared with patients having a higher NIHSS. This suggests that overall, stroke code responders seem to view patients with an NIHSS < 4 as having milder strokes and do not respond with as much urgency as patients with more severe strokes. When examining patients in the subgroup of LKN < 4.5h, we found that at all NIHSS cutoffs we examined (from 1-6), there was a significant difference in CIT between mild and severe strokes. This suggests that with patients in the possible tPA time window, stroke code responders responded differently to mild and severe stroke even at higher NIHSS cutoffs. The PRISMS trial used an NIHSS $\leq$ 5 as the cutoff for mild stroke, which was assigned somewhat arbitrarily[5,6]. Our study gives credence to the idea that milder strokes with this cutoff seem to actually be perceived differently by stroke responders and emphasizes the importance of being aware of differences in the treatment of patients with mild and severe strokes.

Patients presenting with a low NIHSS may have either a small, mild stroke or a large stroke that is misrepresented by the NIHSS. The NIHSS is an imperfect measure of stroke severity because it overemphasizes stroke signs involving the anterior circulation; patients with posterior circulation strokes who may have significant gait abnormalities or vertigo have potentially disabling strokes but a low NIHSS. In previous studies of mild strokes, the definition of severe and mild stroke varies, with cutoffs for mild stroke ranging between 3-10 on the NIHSS[6–9]. Thus we felt it appropriate to examine a range of NIHSS cutoffs to define mild and severe strokes. Across a wide range of NIHSS cutoffs, response times were consistently longer in mild stroke groups, lending support to our hypothesis of a true relationship between NIHSS and response times.

Prior studies examining stroke severity and door-to-imaging times have shown prolonged times in more mild strokes[2,8,9]. Attempts by other groups to improve door-to-imaging times have included relocating the CT scanner closer to the ED, as well as direct delivery of the patient by EMS to the CT scanner[10]. However, few studies have focused on the possibility of stroke code team biases causing differences in response times, which we propose should be examined as a separate time frame to control for triage/registration delays. And indeed, by analyzing CITs, we found inherent responder biases to different levels of stroke severity even after a stroke is recognized, affecting how quickly the stroke code progresses. In addition to identifying imaging delays for patients with mild-appearing strokes after a code has been initiated, we report a threshold effect at an NIHSS of 4 which may better define "mild" strokes. This finding is clinically relevant as it helps provide clarity on quality improvement efforts, emphasizing that improved treatment times for mild stroke is not only dependent on the time prior to recognition of the stroke but what happens following activation of the stroke code.

Both posterior circulation strokes misrepresented by a low NIHSS and true "mild" stroke ultimately need to be treated as seriously as strokes with high NIHSS. An observational study done in 2015 showed that patients with mild strokes (NIHSS $\leq$ 5) benefitted more from tPA administration as compared with no tPA administration[6]. A 2015 retrospective study by the RESUVAL stroke network showed that the long-term benefits of tPA administration in mild strokes (NIHSS $\leq$ 4) were comparable to more serious strokes, and, furthermore, the rate of complications from tPA administration in milder strokes was less than that seen in severe strokes[9]. The risks and benefits of tPA in mild, non-disabling strokes are currently being prospectively assessed in the PRISMS trial[6], which enrolls patients with NIHSS $\leq$ 5. While we could not assess the exact presenting deficit that initiated a stroke code as it was not routinely recorded, it is interesting to note that almost 50% of our cohort had NIHSS $\leq$ 5, consistent with other studies[2,11]. We found that even in the LKW < 4.5h subgroup, the group potentially eligible for treatment with IV tPA, differences persist between mild and severe stroke CITs. Interestingly, we found the largest differences in CIT occurred when using cutoffs involving the mildest strokes (NIHSS of 1-2). This finding further bolsters the importance of the ongoing PRISMS trial, and adds to the literature suggesting that mild strokes are not responded to in the same way as severe strokes even though the benefits of treatment in mild and severe strokes appear to be the same.

Using multivariate analysis, we controlled for only the demographics that might have an impact on first impressions in addition to stroke severity. We did not account for pre-existing deficits in our analysis. However, as old deficits are incorporated into initial NIHSS we do not feel they had a significant impact on our findings. The retrospective nature of the study limits our ability to determine if a CIT delay was attributable to any particular responder-type. We did not assess if these delays led to changes in outcome as measured by administration of tPA in patients with mild stroke. Also, we were not able to analyze the impact of longer code-to-imaging times on outcomes.

In summary, we report a significant delay in CIT based on initial NIHSS score, with a threshold effect at NIHSS=4, not affected by age, sex, or race/ethnicity. No matter how a mild stroke is defined, patients with milder symptoms have been shown not to prompt the same urgency in response as those with more severe stroke syndromes in our study and others[9]. Yet prior studies have shown that a third of mild stroke patients are not discharged home independently[10]. By elucidating inherent responder biases that occur even after a potential stroke has been recognized, we hope our study not only helps to define a possible threshold for mild stroke, but also reminds us that it is imperative that all types of strokes receive equally urgent responses by the medical team.

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