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## **Patient and process factors associated with type of first neuroimaging and delayed diagnosis in childhood arterial ischemic stroke**

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## **Abstract**

**Objectives:** In-hospital factors contribute more to delayed diagnosis of childhood acute ischemic stroke (AIS) than pre-hospital **factors**. We aimed to explore process and patient factors associated with type of and timing to neuroimaging in childhood AIS in the emergency department (ED).

**Methods:** Retrospective hospital registry based study of children with AIS, presenting to an Australian tertiary pediatric ED between January 2003 and December 2012.

Neuroimaging data and timelines of care were also collected from referring hospitals for transferred patients.

**Results:** Seventy-one AIS episodes and 19 transient ischemic attacks (TIA) were recorded. The majority (56%) were initially seen at a referring hospital. Patients **underwent computed tomography (CT) as first scan more frequently** than magnetic resonance imaging (MRI) as first scan (61% vs 32%) at both the referring and tertiary hospitals. Time to first scan as CT was significantly shorter compared with MRI (median 1.5h vs 10.9h;  $p<0.001$ ). MRI was performed more often at the tertiary hospital (92.5% vs 26%,  $p=0.001$ ). Median time to performance of diagnostic MRI was 15.1h (IQR 7.1-23.5), with no significant difference between patients first presenting to a referring hospital and those directly accessing the tertiary center. Patient characteristics including age, past medical history, conscious state, focal symptoms and signs on arrival were not associated with the type of first neuroimaging or time to diagnostic MRI. Patients presenting during weekends were less likely to receive an MRI as first scan (**OR 0.3, 95% CI 0.1-0.8**), while time to

MRI was significantly longer for children presenting after hours (5 pm – 8 am) (median 17.6h vs 8.4h,  $p=0.026$ ). MRI **overall and as first scan** was associated with a higher use of sedation than CT (**OR 6.5, 95% CI 1.3-32.9 and OR 3.9, 95% CI 1.3-11.8**), **particularly** for children younger than 5 years of age (**OR 12.5, 95% CI 3-52.4**).

**Conclusions:** Strategies to improve rapid diagnosis of pediatric stroke should include shared regional hospital networks protocols to optimize local imaging strategies, and where possible rapid transfer to the tertiary center. Future priorities **should** include development of pediatric ED physician decision support tools to differentiate stroke from mimics, and the development and implementation of rapid ED imaging stroke protocols to improve access to confirmatory MRI scanning.

## Introduction

Childhood arterial ischemic stroke (AIS) is an uncommon but potentially devastating condition associated with mortality rates approximating 10% and long-term disability in more than 50% of survivors.<sup>1</sup> Prompt diagnosis of stroke is crucial to guide appropriate management in the acute care setting and increase the feasibility of hyperacute therapies which have been shown to improve outcome in adults.<sup>2-5</sup> However, diagnostic delays in childhood AIS are common and can be a consequence of pre-hospital and in-hospital factors, which include delayed presentation to medical attention, limited clinical recognition of stroke by pediatric physicians, and delayed diagnostic neuroimaging.<sup>6-13</sup>

Computed tomography (CT) is the most commonly employed neuroimaging modality in the emergency setting, due to greater availability and shorter scanning time but it is relatively insensitive to the detection of acute ischemia.<sup>7-10,12</sup> Magnetic resonance imaging (MRI) is the diagnostic gold standard for AIS, being highly sensitive even in the first hours after symptoms onset.<sup>10,12-15</sup>

In order to reduce time to diagnosis in children with AIS and successfully implement pediatric “Code Stroke” protocols, it is important to identify key rate limiting steps following arrival in the ED, which may benefit from development of targeted quality improvement interventions.

The aim of this study was to identify the characteristics of patients and the process factors at referring and tertiary hospitals associated with delayed in-hospital neuroradiological diagnosis of AIS.

## Methods

### Study design

This was a retrospective observational study based on a hospital stroke registry. The study was approved by the Royal Children's Hospital (RCH) Human Research Ethics Committee.

### Study Setting and Population

Stroke episodes in children, aged 1 month to less than 18 years, who presented to the RCH ED with AIS, during the ten-year period from 1<sup>st</sup> January 2003 until 31<sup>st</sup> December 2012, were included. The study population also included transferred children, provided data on timing or type of neuroimaging were available. Referring hospitals included community hospitals and larger general hospitals with emergency departments staffed by pediatric ED physicians, or with inpatient pediatric units where CTs and MRIs were technically available at all times, but pediatric neurologists and anesthesiologists were not. The RCH is the tertiary stroke referral center for the state of Victoria, Australia, meeting recently proposed criteria for a primary pediatric stroke center,<sup>16</sup> with prompt availability of MRI, pediatric anesthesiologists and pediatric neurologists 24/7.

Patients who did not undergo any neuroimaging at either the referring hospital or RCH ED and those with missing data were excluded. **We also excluded patients directly referred from a community hospital to our Neurology Ward or the Pediatric Intensive Care Unit.**

### Study Procedures

Patients with AIS were ascertained from RCH institutional stroke registry, which was established in 2002 to prospectively capture all cases of AIS. Patients were cross-matched with ICD-10 and ED electronic hospital admission database searches to ensure that no cases were missed.

Data extraction was performed for children meeting inclusion criteria using a piloted clinical report form to ensure consistent data collection. Chart abstraction was performed in accordance with previously published guidelines.<sup>17</sup> The abstractor (MD) was not blinded to the study objectives. Data were collected by reviewing the original medical records, as well as the radiological and clinical electronic databases.

## Definitions

AIS was defined as acute onset neurologic deficits lasting more than 24 hours and caused by cerebral ischemia, with neuroimaging showing parenchymal infarction, conforming to known arterial territories and corresponding to the clinical presentation.<sup>18</sup>

Transient ischemic attack (TIA) was defined as transient neurologic deficits in children without neuroimaging evidence of parenchymal infarction. The diagnosis of TIA was made by a pediatric neurologist. Patients with TIA received clinical follow up in order to exclude other causes of brain attack (e.g. hemiplegic migraine, Todd's paralysis). AIS and TIA were combined for the purpose of the analysis.

Diagnostic scan was defined as the neuroimaging modality that led to the diagnosis of AIS.

Level of consciousness was classified using the Glasgow Coma Scale (GCS)<sup>19</sup> and the modified Pediatric GCS (pGCS) for younger-preverbal children.<sup>20</sup>

ED triage urgency was assessed with the national Australian Triage Scale.<sup>21</sup> Patients with Australian Triage Scale categories 1, 2, 3, 4, and 5 are to be treated immediately, within 10, 30, 60, and 120 minutes, respectively.

Timelines of care were defined as follows:

Time from onset to ED arrival: time from onset of symptoms, as reported in the medical notes, to arrival at the ED, as documented in the ED electronic database.

Time from ED arrival to first scan: time from the triage at any ED, as documented in the ED electronic database, to the time of the first neuroimaging study, as reported in the radiology electronic database.

Time from ED arrival to first diagnostic scan: time from the triage at any ED, as documented in the ED electronic database, to the time of the CT or MRI neuroimaging confirming AIS diagnosis, as reported in the radiology electronic database.

## Key outcome measures

The primary outcome was the type and time of performance of initial neuroimaging.

The secondary outcome was the time to neuroradiologic diagnosis of AIS.

## Data Analysis

Categorical variables were reported as percentages for the main findings. Continuous variables were described as median and interquartile range (**IQR**) based on their non-parametric distribution. **Effects of covariates on outcomes have been estimated using a logistic regression (LR) model for binary outcomes and a linear model (LM) for the continuous outcomes. Correlation between events referred to the same patients has been taken into account in the analysis by estimating standard errors of both LR and LM using the Huber-White estimator.**<sup>22</sup> Odds Ratios (ORs) were reported with 95% **confidence interval (CI)**. Differences were considered statistically significant for p values < 0.05 for two-tailed tests. Data were entered into an Excel database (Office version 2007) and were analysed using Stata (version 13.0, StataCorp, College Station, Tex, USA) **and R System**<sup>23</sup> **with the rms libraries.**<sup>24</sup>

## Results

Demographic and clinical characteristics of study population

**During the study period 138 episodes of AIS or TIA occurred. We excluded 36 episodes with direct transfer from a community hospital to the neurology ward or the pediatric intensive care unit. The remaining 102 episodes of stroke occurred in 78 children who presented to the RCH ED.** Of these, twelve episodes were excluded: three children with a past history of radiologically confirmed stroke did not undergo neuroimaging and received a clinical diagnosis of TIA, six because diagnostic neuroimaging was performed before the arrival in the ED, and three because of missing data. The remaining 90 episodes were considered the study population.

Median age at presentation was 7.4 years (IQR 3.5-11.5), the majority were females, 56 (62%), and median GCS on arrival to hospital was 15 (IQR 14-15). The characteristics of the study population are reported in Table 1.

The majority of children were referred to RCH from another hospital (56%), and arrived by ambulance (64%) to our tertiary center.

Thirty nine percent were previously healthy and almost a quarter had a history of previous stroke (22%). Sixty-six patients (73%) presented during weekdays and 46 (51%) presented between 8 am and 5 pm.

The final diagnosis was AIS in the great majority of patients (79%), while 21% received the final diagnosis of TIA.

#### Neuroimaging studies

All patients received at least one neuroimaging study during their evaluation at the referring hospital or RCH. Overall 58 (64%) children underwent a CT as the initial neuroimaging modality, which was diagnostic in only 24% of cases. A CT scan was performed in 30/50 (60%) of patients who presented to a referring hospital, versus 25/40 (62.5%) of patients who directly presented to RCH ( $p=0.06$ ). Thirteen (26%) children seen at a referring hospital were transferred without performing any neuroimaging. Of these, three received a CT scan as initial neuroimaging at the tertiary center. The comparison of patients' characteristics and their initial management at referring hospital and tertiary center is detailed in Table 2.

Seventy-three patients (81%) underwent an MRI, which was the initial neuroimaging modality in only 32 (36%) patients. The great majority 68% was performed at the tertiary center, while only 26% of patients seen at a referring hospital received an MRI, and only 14% of the patients presenting to a referring hospital received an MRI as first scan. Forty-one patients with an initial negative CT required MRI for definitive diagnosis. Overall sedation was more frequently used for children undergoing MRI than those undergoing CT (41% vs 12%,  $p<0.001$ ).

Seventy-seven patients (86%) received a diagnosis based on positive neuroradiological findings consistent with either AIS or TIA: abnormal CT in 14 (18%) patients and abnormal MRI in 63 (82%) patients. In 13 patients the diagnosis of TIA was made by a pediatric neurologist based on clinical assessment and follow up in the absence of abnormal neuroimaging findings.

#### Time to neuroimaging and diagnosis

The time from symptom onset to hospital arrival was similar between patients initially presenting to the referring center and those presenting to the tertiary hospital. Time from hospital arrival to first scan for the whole group was 3.3 hours (IQR 1.2-8.3) and to diagnostic scan was 11.3 hours (IQR 4.1-22.5). Time to CT was shorter when performed in a referring hospital (1 hour, IQR 0.8-1.5 vs 1.7 hours, IQR 1.2-3.9;  $p=0.035$ ). Overall the median time to the first scan was significantly shorter when CT

was performed, compared with MRI (1.5 hours, IQR 1-3.7 vs 10.9 hours, 4.3-21.5;  $p<0.001$ ).

The time from hospital presentation (either referring or tertiary hospital) to MRI scan, when performed, was overall 15.1 hours, IQR 7.1-23.5 hours, and was similar for patients who first presented to a referring hospital compared with those who directly presented to the tertiary center (15.7 hours, IQR 7.6-24.9 vs 13.9 hours, IQR 5.2-22.6;  $p=0.176$ ).

Patient and process factors associated with delayed in-hospital diagnosis

The comparison of characteristics between patients who received CT and MRI as the initial neuroimaging modality is reported in Table 3.

Patient characteristics such as age, past medical history, GCS on arrival or focal symptoms and signs were not associated with the type of first neuroimaging or time to diagnostic MRI (Table 4).

Children who underwent MRI overall and as first scan were more likely to need sedation (**OR 6.5, 95% CI 1.3-32.9 and OR 3.9, 95% CI 1.3-11.8**). Age younger than 5 years (**OR 12.5, 95% CI 3-52.4**) was associated with significantly increased use of sedation. Patients presenting during weekends were less likely to receive MRI as first scan (**OR 0.3, 95% CI 0.1-0.8**).

Complete data about timing from hospital arrival to diagnostic MRI was available for 64 patients (83%). Analysis of MRI timing according to patients' and process factors are reported in Table 4. Performance of **diagnostic** MRI was significantly delayed in children presenting to the ED after hours (5 pm-8 am,  $p=0.026$ ).

## Discussion

Our study provides insight into patient and process factors contributing to delayed diagnostic neuroimaging in children with acute AIS. Few pediatric studies have explored patients and in-hospital care process factors contributing to delayed diagnosis, and our study provides further insight in the timing of imaging for pediatric AIS within a regional care network..

The American Heart Association guidelines recommend completion of diagnostic imaging within 45 minutes of arrival to the ED in adults with suspected AIS.<sup>25</sup> Early

performance of diagnostic neuroimaging is essential to increase access to hyperacute therapies, and to normalize physiological parameters to prevent further injury to at risk penumbral tissue. Correct early radiological diagnosis of stroke has been shown to be associated with reduced costs, increased likelihood of independent survival and more quality adjusted life years in adults.<sup>26</sup>

We found no association between patient factors including age, stroke risk factors, past medical history, conscious state and presenting clinical features, and the type of first neuroimaging or the time to diagnostic MRI. This may relate to limited awareness or knowledge of pediatric stroke among pediatric ED physicians and lack of available local resources to make a timely diagnosis. While our tertiary care center has a 24/7 MRI and anesthetist service availability, more than half of the study sample initially presented to a referring hospital, where these resources may not be available.

Our findings confirm that in-hospital factors play an important role in contributing to delayed AIS diagnosis.<sup>8,12</sup> In accordance with previous studies, CT is the most common first neuroimaging modality at referring hospitals and the tertiary center.<sup>8,10,12</sup> The median time of 3.3 hours to first scan (CT in nearly two thirds of cases) in our study, is similar to a recent UK study,<sup>12</sup> but much greater than reported in adults.<sup>26</sup> CT is more easily available in the ED, but its poor sensitivity is a major contributor to delayed AIS diagnosis.<sup>7-10,12</sup> In the study by Mallick et al., diagnosis of AIS was delayed especially when the first neuroimaging was a non diagnostic CT scan.<sup>12</sup> In our study an initial CT scan was not informative in 76% of patients.

Time to CT scan was shorter at referring hospitals. Similarly, although only 10% of children presenting to referring hospitals received an MRI, there was a trend towards shorter time to MRI compared with our tertiary care center. However, it is unclear which factors may contribute to these differences. While MRI was performed less often at referring hospitals, there was no difference in the overall time to MRI at the tertiary care center between transferred and direct access patients. A low index of suspicion of ED physicians for AIS may partly explain this finding. In our sample the median time from arrival to diagnostic scan (11.3 hours), was half that reported in a population based study from the United Kingdom (20.4 hours), but well beyond the window for a hyperacute therapy. In contrast to the U.K. study, the performance of a non-diagnostic CT did not seem to significantly affect the time to MRI.<sup>12</sup> The small sample size, and differences in study populations may explain this difference.

Overall, MRI was less likely to be performed as first neuroimaging modality during weekends and time to MRI was longer when performed outside working hours. Although sedation was associated with type of first neuroimaging modality, being more frequently required for MRI, it was not associated with longer time to MRI. This suggests sedation alone might not be a major barrier to delayed MRI. However, rapid MRI protocols may significantly reduce time to MRI in patients with AIS. Recent studies have demonstrated the feasibility of rapid MRI screening protocols in children which avoid the need for anesthesia in young children.<sup>28,29</sup>

Diffusion-weighted MRI more reliably detects early brain ischemia than CT<sup>30</sup> and is recommended in evidence based guidelines as the imaging modality of choice in adults with stroke presenting less than 12 hours from symptoms onset.<sup>31</sup> Several studies have demonstrated the feasibility and excellent diagnostic accuracy of rapid MRI imaging in adults being considered for tissue plasminogen activator.<sup>32-34</sup>

Technological advances which include parallel data acquisition and echo planar imaging have decreased MRI scanning times to 6-15 minutes.<sup>34</sup> MRI imaging did not result in longer delay to initiation of treatment<sup>35</sup> and informed management decisions more effectively than CT imaging in one adult study. MRI usage enabled treatment of patients with mild symptoms and seizures, who might have otherwise been misdiagnosed. Another recent U.S. study reported a reduction of 40% in median door to needle time in adults screened with MRI for rapid stroke treatment.<sup>33</sup> Of equal importance, a short diffusion weighted MRI differentiated stroke from stroke mimics in adults in the ED setting,<sup>32</sup> and it influenced decision making in 4 patients with extensive infarction and in 10 patients with stroke mimics. This finding is particularly relevant to children given the lower a priori probability of stroke.<sup>11,28</sup>

Our study highlights several in-hospital factors, which would benefit from targeted quality improvement initiatives to achieve earlier diagnosis of pediatric AIS.

Given that more than half of our patients initially presented to a referring hospital shared regional pediatric stroke protocols that take into account the strengths and weaknesses of the regional hospital network should be developed and implemented. Such protocols should consider local resource availability and transport-related challenges, as well as promote strategies to increase ED physicians' awareness and knowledge on the signs and symptoms of pediatric AIS and the potential benefits of time critical treatments such as thrombolysis. Implementation of 'Code Stroke'

protocols in pediatric tertiary care centers should be pursued to warrant easy access to rapid screening MRI sequences 24/7, as well as ready availability of neurologists, anesthesiologists, and radiologists.

A recent study from the U.S. has demonstrated the diagnostic and therapeutic usefulness of developing and implementing a pediatric acute stroke protocol. Activation of the protocol resulted in selection of MRI as the first imaging modality in 76% of children within a median time of 94 minutes from hospital arrival.<sup>28</sup> Furthermore, the protocol resulted in one-tenth of AIS patients undergoing thrombectomy or thrombolysis. Other benefits included the identification of a further 14% of children with non-stroke neurological conditions who required urgent intervention.

Finally, programs to educate emergency physicians have been shown to be effective in improving accuracy of clinical stroke diagnosis in adults,<sup>36</sup> and should be implemented in pediatric hospitals.

**Overall, in order to reduce the delay from symptoms onset to diagnostic neuroimaging, future efforts should be directed towards improving public and physician awareness on childhood stroke, developing coordinated systems of care, which include regional hospital network protocols for rapid transfer to the tertiary centers with capability for hyperacute interventions, decision-support tools to guide ED physician decisions about the choice of urgent neuroimaging, and internal protocols to expedite access to rapid MRI sequences.**

The study has some limitations. We were unable to assess the factors influencing ED physicians' decision-making process. Therefore it was not possible to determine whether timing and selection of particular imaging modality was affected by factors such as the clinician's provisional diagnosis, including suspicion of stroke, availability of CT or MRI, the need for sedation or availability of pediatric anesthesiology. We could not assess the influence of patient factors such as presence of diffuse or focal signs, or the severity of symptoms, on type of or time to first imaging. We chose not to assess contributors to delayed imaging in children who were inpatients when the stroke occurred, but we included children presenting to the ED with past history of stroke. This was not a population-based study and therefore the findings may not be applicable to a broader population of children with AIS. **We did not determine an a**

priori sample size to ensure detection of true significant differences, as the primary focus of our project was observational with the aim of conducting an exploratory analysis on data collected by the hospital stroke registry since its inception. Although few previous studies analyzed factors associated with delayed pediatric AIS diagnosis<sup>8,9,12</sup> none has so far specifically focused on the acute care setting evaluating both patient and process factors potentially related to delayed diagnosis within a hospital regional network. In addition, the low frequency of the condition studied and the setting of interest, makes it challenging to include a large sample of patients. Despite this limitation we believe that our data may contribute to the development of future studies focusing on quality improvement initiatives for more rapid pediatric stroke diagnosis.

The strengths of this study were that we explored process of care factors and differences in timelines of care between referring hospitals and the tertiary care center.

## Conclusions

The majority of children with AIS first present to a non-tertiary care pediatric center. CT remains the first neuroimaging modality in patients with AIS presenting to the acute care setting, despite its low diagnostic accuracy. Based on our results, strategies to improve rapid diagnosis of pediatric stroke should include regional hospital network protocols to optimize local imaging strategies, and rapid transfer to the tertiary center. Development of pediatric ED physician decision support tools to identify children with a high probability of stroke and implementation of rapid ED MRI stroke protocols are required to improve access to interventions to minimize extent of brain injury. Future research should also assess the effects of implementation of these interventions on patients' outcome.

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**Table 1. Demographic and Clinical Characteristics of Patients with Acute Ischemic Stroke (n=90)**

| Variable   | n  | %  |
|--|----|----|
| <b>Age groups</b>                                |    |    |
| ≤ 5 years  | 38 | 42 |
| >5 years   | 52 | 58 |
| <b>Gender</b>                                    |    |    |
| Male   | 34 | 38 |
| <b>GCS</b>                                       |    |    |
| 15-13  | 78 | 87 |
| 12-9   | 11 | 12 |
| ≤ 8  | 1  | 1  |
| <b>Hospital of presentation</b>                  |    |    |
| First seen at tertiary care hospital             | 40 | 44 |
| First seen at referring hospitals                | 50 | 56 |
| <b>Triage category for referred patients*</b>    |    |    |
| <b>(n=50)</b>                                    |    |    |
| 1+2+3  | 48 | 96 |
| 4+5  | 2  | 4  |
| <b>Triage category for direct access to XXX*</b> |    |    |
| <b>(n=40)</b>                                    |    |    |
| 1+2+3  | 36 | 90 |
| 4+5  | 4  | 10 |
| <b>Mode of arrival</b>                           |    |    |
| Ambulance transport                              | 58 | 64 |
| No ambulance transport                           | 32 | 36 |
| <b>Past medical history</b>                      |    |    |
| Healthy  | 35 | 39 |
| Previous stroke                                  | 20 | 22 |
| Head/neck trauma                                 | 9  | 10 |
| Infection (incl. chickenpox)                     | 6  | 7  |
| Migraine/Headache                                | 2  | 2  |
| Family history of stroke                         | 3  | 3  |
| Cardiac disease                                  | 4  | 4  |
| Known CVD/malformation                           | -  | -  |
| Others   | 11 | 12 |
| <b>Day of presentation<sup>#</sup></b>           |    |    |
| Weekdays   | 66 | 73 |

|   |    |    |
|---|----|----|
| Weekends                                |    |    |
| <b>Time of presentation<sup>#</sup></b> |    |    |
| Working hours (8 am-5 pm)               | 46 | 51 |
| Non working hours (5 pm-8 am)           | 36 | 40 |
| Unknown <sup>^</sup>                    | 8  | 9  |
| <b>Final diagnosis</b>                  |    |    |
| AIS                                     | 71 | 79 |
| TIA                                     | 19 | 21 |

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AIS = acute ischemic stroke, IQR = interquartile range, GCS = Glasgow Coma Scale

ED = emergency department, GP= general practitioner, CVD = cerebro vascular disease

\*Triage categories at XXX: see methods section

#Date and time of presentation at the first hospital presentation

^All patients presenting to a referring hospital

°Seven patients with a previous history of stroke whose final clinical diagnosis was transient ischaemic attack

§Opioids given alone were not regarded as sedation.

**Table 2. Clinical Characteristics and management of patients initially presenting at referring hospitals and**

| <b>Variable</b>          | <b>Referring hospitals<br/>(n=50)</b> | <b>Tertiary care center<br/>(n=40)</b> | <b>p</b>     |
|--------------------------|---------------------------------------|--|--------------|
| <b>Age (median, IQR)</b> | 7.72, 3.54-12.02                      | 6.64, 3.24-11.26                       | <b>0.484</b> |
| <b>Gender, n (%)</b>     | 21 (42)                               | 12 (30)                                | <b>0.285</b> |

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Tertiary care center

|  |                     |                       |                  |
|--|---------------------|-----------------------|------------------|
| Male   |                     |                       |                  |
| <b>GCS, n (%)</b>                                |                     |                       |                  |
| 15-13  | 45 (90)             | 33 (82.5)             |                  |
| ≤ 12   | 5 (10)              | 12 (17.5)             | <b>0.434</b>     |
| <b>Past medical history, n (%)</b>               |                     |                       |                  |
| Previously healthy                               | 29 (58)             | 17 (42.5)             |                  |
| Risk factors for stroke <sup>°</sup>             | 21(42)              | 23 (57.5)             | <b>0.190</b>     |
| <b>Day of presentation, n (%)</b>                |                     |                       |                  |
| Weekdays   | 35 (70)             | 31 (77.5)             |                  |
| Weekends   | 15 (30)             | 9 (22.5)              | <b>0.462</b>     |
| <b>Time of presentation, n (%) n=82</b>          |                     |                       |                  |
| 8 am-5 pm  | 27 (64)             | 19 (47.5)             |                  |
| 5pm-8 am   | 15 (36)             | 21 (52.5)             | <b>0.136</b>     |
| <b>Initial Neuroimaging modality*, n (%)</b>     |                     |                       |                  |
| CT   | 30 (60)             | 25 (62.5)             |                  |
| MRI  | 7 (14)              | 15 (37.5)             | <b>0.060</b>     |
| <b>Total MRI performed, n (%)</b>                | 13 (26)             | 37 (92.5)             | <b>&lt;0.001</b> |
| <b>Timelines of care in hours (median, IQR)§</b> |                     |                       |                  |
| Symptom onset to hospital presentation           | 2.8, 1-19 (n=46)    | 3.6, 1.3-18.5 (n=40)  | <b>0.196</b>     |
| Hospital presentation to CT as first scan        | 1, 0.8-1.5 (n=15)   | 1.7, 1.2-3.9 (n=25)   | <b>0.035</b>     |
| Hospital presentation to MRI as first scan       | 4.3, 3-16.6 (n=5)   | 8.9, 3.2-16.6 (n=15)  | <b>0.884</b>     |
| Hospital presentation to MRI as diagnostic scan  | 3.6, 1.6-16.6 (n=6) | 13.9, 5.2-22.6 (n=30) | <b>0.176</b>     |
| <b>Final diagnosis, n (%)</b>                    |                     |                       |                  |
| AIS  | 41 (82)             | 30 (75)               |                  |
| TIA  | 9 (18)              | 10 (25)               | <b>0.419</b>     |

IQR = interquartile range, GCS = Glasgow Coma Scale, CT = computed tomography, MRI = magnetic resonance imaging

AIS = acute ischemic stroke, TIA = transient ischemic attack

<sup>°</sup>Presence of any of these: head/neck trauma, recent infection, family history of stroke, cardiac disease, autoimmune disease, malignancy/chemotherapy, past history of stroke

\*No neuroimaging performed in 13 patients initially presenting to a referring hospital

§Data on timelines of care available

**Table 3. Factors associated with type of first imaging**

|   | <i>CT as first scan<br/>(n=58)</i> | <i>MRI as first scan<br/>(n=32)</i> | <i>p</i>     | <i>OR, 95% CI</i>    |
|---|------------------------------------|-------------------------------------|--------------|----------------------|
| <b>Age groups, n (%)</b>                            |                                    |                                     |              |                      |
| ≤ 5 years   | 25 (43)                            | 13 (41)                             |              |                      |
| > 5 years   | 33 (57)                            | 19 (59)                             | <b>0.828</b> | <b>0.9, 0.4-2.3</b>  |
| <b>Past medical history, n (%)</b>                  |                                    |                                     |              |                      |
| Risk factors for stroke*                            | 26 (45)                            | 18 (55)                             |              |                      |
| Healthy   | 32 (55)                            | 14 (45)                             | <b>0.266</b> | <b>1.6, 0.7-3.6</b>  |
| <b>GCS, n (%)</b>                                   |                                    |                                     |              |                      |
| 15-13   | 48 (83)                            | 30 (94)                             |              |                      |
| ≤ 12  | 10 (17)                            | 2 (6)                               | <b>0.160</b> | <b>0.3, 0.1-1.6</b>  |
| <b>Focal symptoms and signs<sup>o</sup>, n (%)</b>  |                                    |                                     |              |                      |
| Yes   | 54 (93)                            | 29 (91)                             |              |                      |
| No  | 4 (7)                              | 3 (9)                               | <b>0.654</b> | <b>1.4, 0.3-6</b>    |
| <b>Initial presenting Hospital, n (%)</b>           |                                    |                                     |              |                      |
| Referring   | 33 (57)                            | 17 <sup>**</sup> (53)               |              |                      |
| Tertiary care                                       | 25 (43)                            | 15 (47)                             | <b>0.707</b> | <b>1.2, 0.5-2.6</b>  |
| <b>Day of presentation, n (%)</b>                   |                                    |                                     |              |                      |
| Weekdays  | 38 (66)                            | 27 (87)                             |              |                      |
| Weekends  | 20 (34)                            | 5 (13)                              | <b>0.019</b> | <b>0.3, 0.1-0.8</b>  |
| <b>Time of presentation, n (%)</b>                  |                                    |                                     |              |                      |
| 8 am – 5 pm   | 28 (48)                            | 18 (56)                             |              |                      |
| 5 pm – 8 am   | 25 (43)                            | 11 (34)                             | <b>0.427</b> | <b>0.7, 0.3-1.7</b>  |
| <b>Sedation<sup>§</sup> (n=80, 52 vs 28), n (%)</b> |                                    |                                     |              |                      |
| Not sedated   | 45 (87)                            | 18 (62)                             |              |                      |
| Sedated   | 7 (13)                             | 11 (38)                             | <b>0.014</b> | <b>3.9, 1.3-11.8</b> |

CT = computed tomography, MRI = magnetic resonance imaging, GCS = Glasgow Coma Scale, IQR = interquartile range

<sup>o</sup>Presence of focal symptoms and signs defined as one of the following: any of facial palsy/weakness, arm/leg weakness and speech impairment.

\*Presence of any of: head/neck trauma, recent infection, family history of stroke, cardiac disease, autoimmune disease, malignancy/chemotherapy, past history of stroke.

<sup>§</sup>Opioids given alone were not regarded as sedation.

\*\*10 patients received MRI as first scan at the tertiary center after transfer

**Table 4. Factors associated with time to diagnostic MRI**

|  | <i>Time to diagnostic MRI<br/>Median, IQR</i> | <i>p</i>     |
|--|---|--------------|
| <b>Age groups (n=64, 22 vs 42), n (%)</b>                          |   |              |
| ≤ 5 years  | 15.5, 6.0-23.7                                | <b>0.981</b> |
| > 5 years  | 14.9, 7.5-23.2                                |              |
| <b>Past medical history (n=64, 30 vs 34), n (%)</b>                |   |              |
| Risk factors for stroke*   | 16.9, 8.9-22.8                                | <b>0.916</b> |
| Healthy  | 12.7, 4.7-24.9                                |              |
| <b>GCS (n=64, 55 vs 9), n (%)</b>                                  |   |              |
| 15-13  | 14.5, 6.6-23.2                                | <b>0.932</b> |
| ≤ 12   | 16.6, 10.9-24.0                               |              |
| <b>Focal symptoms and signs<sup>o</sup> (n=64, 59 vs 5), n (%)</b> |   |              |
| Yes  | 14.8, 7.5-22.8                                | <b>0.721</b> |
| No   | 24.4, 6.6-25.7                                |              |
| <b>Initial presenting Hospital (n=64, 34 vs 30), n (%)</b>         |   |              |
| Referring  | 15.5, 7.6-24.9                                | <b>0.391</b> |
| Tertiary care  | 13.9, 5.2-22.6                                |              |
| <b>Day of presentation (n=64, 48 vs 16), n (%)</b>                 |   |              |
| Weekdays   | 16.4, 6.8-23.6                                | <b>0.836</b> |
| Weekends   | 14.2, 7.1-21.4                                |              |
| <b>Time of presentation (n=64, 36 vs 28), n (%)</b>                |   |              |
| 8 am – 5 pm  | 8.4, 4.5-23.6                                 | <b>0.026</b> |
| 5 pm – 8 am  | 17.6, 13.9-23.5                               |              |
| <b>Performance of non-diagnostic CT (n=64, 35 vs 29), n (%)</b>    |   |              |
| Yes  | 17.6, 9.5-24                                  | <b>0.244</b> |
| No   | 10.9, 4.3-21.5                                |              |
| <b>Sedation for MRI § (n=61, 35 vs 26), n (%)</b>                  |   |              |
| Unsedated  | 14.5, 7.6-23.2                                | <b>0.454</b> |
| Sedated  | 16.4, 6.0-24.0                                |              |

CT = computed tomography, MRI = magnetic resonance imaging, GCS = Glasgow Coma Scale, IQR = interquartile range

<sup>o</sup>Presence of focal symptoms and signs defined as one of the following: any of facial palsy/weakness, arm/leg weakness and speech impairment.

\*Presence of any of these: head/neck trauma, recent infection, family history of stroke, cardiac disease, autoimmune disease, malignancy/chemotherapy, past history of stroke.

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§Opioids given alone were not regarded as sedation.

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