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37 JR: Acquisition and interpretation of clinical data, agreement to be accountable for all aspects of
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39 CH: Acquisition and interpretation of clinical data, agreement to be accountable for all aspects of
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41 LH: Acquisition and interpretation of clinical data drafted initial manuscript, agreement to be
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43 GJ: Conceived the manuscript, analyzed the data, critically reviewed final manuscript.

44 AYP: Conceived the manuscript, analyzed the data, critically reviewed final manuscript.

45 YD: Conceived the manuscript, analyzed the data, drafted the initial manuscript, agreement to be
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47 AVC: Conceived the manuscript, analyzed the data, drafted the initial manuscript, agreement to
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49 **Abstract:**

50 **Background:** Patients with stroke while hospitalized experience important delays in symptom
51 recognition. This study aims to describe the overall management of an in-hospital stroke
52 population and how it compares with out-of-hospital community onset stroke population.

53 **Methods:** In this retrospective observational study, we included consecutive patients with in-
54 hospital and out-of-hospital strokes (both ischemic and hemorrhagic) over a period of one year
55 treated at a comprehensive stroke center. Demographic and clinical data were extracted, and
56 patient groups were compared with regards to stroke treatment times metrics. **Results:** 362
57 patients diagnosed with acute stroke were included, of whom 38 (10.5%) had in-hospital and 324
58 (89.5%) had out-of-hospital strokes. The median delay to stroke recognition (time between the
59 last time seen well and first time seen symptomatic) was significantly longer in in-hospital
60 compared to out-of-hospital strokes (77.5 (0-334.8) versus 0 (0-138.5) minutes, $p = 0.04$). The
61 median time interval from stroke code activation to arrival of the stroke team at bedside was
62 significantly shorter in in-hospital versus out-of-hospital cases (10 (6-15) versus 15 (8-24.8)
63 minutes, $p = 0.01$). In-hospital strokes were less likely to receive thrombolysis (12.8% versus
64 45.4%, $p < 0.01$) with a significantly higher mortality (18.2% versus 2.6%, $p < 0.01$) and longer
65 overall median hospital stay (3 (1-7) versus 12 days (7-23), $p < 0.01$) compared to out-of-hospital
66 strokes. **Conclusion:** This study showed significant delays in stroke symptom recognition and
67 stroke code activation for in-hospital stroke patients despite comparable overall stroke time
68 metrics. Development of in-hospital stroke protocols and systematic staff training on stroke
69 symptom recognition should be implemented to improve care for hospitalized patients.

70 **Introduction**

71 In-hospital strokes account for approximately 6.5% to 15% of all strokes but are associated with
72 higher mortality, extended hospitalization, and less rehabilitation potential.¹⁻³ Patients who suffer
73 an stroke while being hospitalized often have many comorbidities, including thromboembolic
74 risk factors.^{1,4,5} Medical procedures and surgery also confer a higher risk of stroke.⁶ Management
75 of strokes during hospital stay is challenging as many confounding factors such as delirium,
76 immobilization, or sedation may contribute to delays in the recognition of stroke symptoms.
77 Comorbid conditions, functional status and post-surgical bleeding risks can limit eligibility for
78 thrombolysis. Compared to out-of-hospital strokes, strokes in hospitalized patients are associated
79 with a less guideline-based stroke treatment from the medical team.³ Intracerebral hemorrhage
80 (ICH) can also occur in-hospital and is associated with higher mortality than ischemic stroke.⁷
81 While patients with ICH cannot benefit from acute reperfusion therapies, rapidly lowering blood
82 pressure, reversing anticoagulation, controlling blood sugar levels and treating fever can improve
83 functional outcomes and these patients should also be managed urgently.⁸⁻¹⁰ Delays in diagnosis
84 and treatment should be shortened as much as possible to optimise patient outcomes.

85 The **Diagnosis and Evaluation of stroke in-hospital and in the community (DELAY)** study
86 aims to describe the in-hospital stroke population at a single comprehensive stroke center and
87 compare their baseline characteristics, time metrics and treatment with out-of-hospital stroke
88 patients to identify areas for possible improvement.

89 **Methods**

90 We conducted a single-center, retrospective cohort study of all acute ischemic or hemorrhagic
91 strokes that occurred between November 27th, 2017 and November 27th, 2018, at a large
92 academic comprehensive stroke center in Montreal, Canada. Patient data was retrieved by
93 hospital chart review by medical archivists using ICD codes including cases with stroke as a
94 final diagnosis or as a complication of hospitalization. In addition, cases were identified by a
95 review of the electronic patient record which includes data from all acute stroke codes evaluated
96 by the vascular neurology team – the MONTreal Neurovascular and StrokE data Repository
97 (MONSTER).

98 We excluded patients with subacute out-of-hospital strokes (patients with last seen well to first
99 seen symptomatic delay of more than 24 hours), stroke mimics, transient ischemic attack, and

100 patients initially evaluated in another center and transferred for thrombectomy. After a review of
101 imaging reports, patients in whom the acute stroke was an incidental finding were excluded.

102 *Patient characteristics*

103 Baseline patient characteristics including the type of stroke (hemorrhagic or ischemic) and prior
104 use of antithrombotic treatment were documented. Medical or surgical procedures in the days
105 preceding stroke were recorded.

106 *Stroke time metrics*

107 We used a standardized data collection form in all acute stroke cases assessed by the
108 neurovascular team. The time of imaging was calculated using the time recorded at the start of
109 acute neurovascular imaging. The time of thrombolysis was defined as the time of administration
110 of an intravenous bolus of thrombolysis. The time of thrombectomy was defined as the time of
111 initial arterial puncture in the angiography suite.

112 *Statistical analysis*

113 We summarized baseline characteristics using descriptive statistics such as median and
114 interquartile ranges (IQR) or frequencies (proportions) where appropriate. We performed
115 univariable comparisons of the median time intervals from last time seen well to first seen
116 symptomatic, stroke code activation, stroke team arrival at bedside, imaging, and treatment
117 initiation (thrombolysis, thrombectomy) using either Chi-square test or Fischer Exact test (with
118 expected cell frequencies less than 5) for nominal data and the Mann-Whitney U test for ordinal
119 data with a cutoff for statistical significance of 0.05. The analyses were performed using
120 Statistical Package for Social Sciences (SPSS) version 27(Armonk, NY).

121 **Results**

122 A total of 362 patients were diagnosed with an acute stroke during the study period. Thirty-eight
123 patients (10.5%) had strokes in-hospital while 324 (89.5%) had out-of-hospital strokes as seen in
124 Figure 1. The demographic features and comorbidities of each group are presented in Table 1.
125 Both groups were comparable in terms of conventional cerebrovascular risk factors except for a
126 higher prevalence of history of cancer in the in-hospital group ($p = 0.02$). Anticoagulation was
127 stopped for a medical procedure in significantly more in-hospital patients as compared to the out-
128 of-hospital treatment group. Among the 38 in-hospital patients, 23 underwent a procedure shortly
129 before their stroke (60.5%) (Table 2).

130 Among the 324 out-of-hospital patients, 74% were assessed by the stroke team within 4.5 hours
131 of the last time seen well compared to 57% in the in-hospital group ($p = 0.03$). In the out-of-
132 hospital group, 45.4% received thrombolysis compared to 12.8% in the in-hospital group ($p =$
133 0.02). In terms of stroke time metrics as shown in Table 2, the median delay to stroke onset
134 recognition (time between the last time seen well and first time seen symptomatic) was 77.5 (0-
135 334.8) minutes in hospitalized patients and 0 (0-138.5) minutes, in out-of-hospital patients ($p =$
136 0.04), presumably because more out-of-hospital strokes were witnessed at onset. After stroke
137 recognition, the time to stroke code activation was similar for in-hospital and out-of-hospital
138 cases (60 (25-141) versus 58 (37-107.8) minutes, $p = 0.72$). On the other hand, the median time
139 interval from stroke code activation to arrival of the stroke team at the bedside of the patient was
140 significantly shorter in hospitalized patients compared to out-of-hospital patients (10 (8-15)
141 versus 15 (8-24.8) minutes, $p = 0.01$). Time to imaging and treatment initiation including
142 thrombolysis and thrombectomy were similar between groups. Out-of-hospital patients were
143 significantly more likely to receive thrombolysis (45.4% versus 12.8 %, $p < 0.01$) whereas
144 thrombectomy rates were not statistically different in both groups (24.4% versus 12.8%, $p =$
145 0.12).

146 The proportion of patients with ICH was similar in both the in-hospital and out-of-hospital
147 groups (10.5% and 10.8%). Among in-hospital patients with ICH, 3 of 4 (75%) had a recent
148 procedure (nephrectomy, carotid endarterectomy, and mitral valve replacement). Regarding
149 acute ICH management of hospitalised patients, 2 out of 4 (50%) received intravenous blood
150 pressure lowering therapy (one before and one after the arrival of the stroke team), while 2 out of
151 4 (50%) did not need any change in their medication. All 4 hospitalised patients with ICH died
152 during hospitalization. For out-of-hospital patients with ICH, only 4 out of 35 (11%) patients did
153 not receive any intravenous blood pressure lowering therapy, and 10 (29%) died while
154 hospitalized.

155 Patients with in-hospital stroke included those with and without varied invasive procedures prior
156 to the incident stroke (Table 3 and Table 4). The code stroke was not called for 9 in-hospital
157 stroke patients (23.7%) and specific reasons could not be identified on retrospective review of
158 the case records. In-hospital patients had a significantly higher mortality (12.0% versus 36.0 %, $p < 0.01$) and longer overall median hospital stay (3 (1-7) versus 12 (7-23) days, $p < 0.01$) than out-
159 of-hospital patients.
160

161 **Discussion**

162 In this observational, retrospective cohort study comparing in-hospital and out-of-hospital
163 patients at our comprehensive stroke center, we found significantly longer delays for stroke
164 symptom recognition in hospitalised patients with similar time intervals to stroke code activation
165 in both groups. There were no statistically significant differences in the overall management
166 times after activation of the stroke team.

167 *Stroke recognition delays*

168 A possible explanation for the significantly longer delay in stroke symptom recognition in
169 hospitalized versus out-of-hospital cases is that most patients in the community recognized their
170 symptoms immediately by themselves or had a witnessed stroke onset with rapid emergency
171 medical service activation by bystanders. Contrarily, hospitalized patients may be less alert or
172 have other conditions masking their stroke symptoms and may have onset of stroke while
173 unsupervised in their room. We can infer that valuable time is lost in hospitalized stroke patients
174 due to delays in the recognition of stroke symptoms. It is also important to acknowledge that
175 there may be patients with out-of-hospital strokes who may not have been appropriately referred
176 to stroke team irrespective of stroke code activation.

177 A delay in timely stroke recognition among in-hospital patients has been found several other
178 studies.¹¹⁻¹³ Akbik et al. (2020) determined that fewer than 30% of patients were assessed within
179 ninety minutes, and more than 25% were not seen within 12 hours of symptom recognition.¹¹ In-
180 hospital stroke patients may be subject to significantly longer delays from onset to imaging and
181 from imaging to treatment.¹² A large Canadian cohort comparing stroke care delivery and
182 outcome for 973 patients with in-hospital strokes and 28 837 patients with out-of-hospital strokes
183 revealed significantly longer times in symptom recognition among in-hospital patients, with a
184 smaller proportion undergoing brain imaging.¹³

185 Several hypotheses could help explain these findings. First, public awareness campaigns have
186 been focused on FAST signs and symptoms recognition in the community¹⁴, but the same efforts
187 have not been devoted to training hospital personnel for acute stroke detection.¹⁵ Delays in stroke
188 code activation for hospitalized patients may also stem from infrequent patient evaluations by
189 staff, particularly among patients considered stable, and absence of families or caregivers at the
190 bedside. Secondly, many symptoms can be misattributed to another comorbid condition. For
191 example, speech disturbance, drowsiness or dizziness can be erroneously associated with

192 medication use, a post-surgical state, or delirium.^{1,16} Paresis can also go unnoticed in a bedridden
193 patient if there is no standardized screening for neurological deficits by clinical staff.

194 *Stroke code activation*

195 We observed similar time intervals to stroke code activation in hospitalized and out-of hospital
196 stroke patients even though this delay should presumably be shorter given that they are
197 surrounded by healthcare staff. It is also concerning that the stroke team was not notified for 9 of
198 the 38 in-hospital stroke patients (23.7%), thereby limiting their access to acute reperfusion
199 therapy. A possible explanation may be that seven out of nine patients had recent surgery
200 (77.8%) which may have been deemed an automatic contra-indication to thrombolysis by the
201 treating medical team – but in which case urgent neurovascular evaluation would still be
202 indicated, to consider patient eligibility for endovascular thrombectomy.

203 Others have also reported delayed stroke team activation even after recognition of a possible
204 stroke by medical staff in hospitalised patients,¹² which may in part be due to the absence of
205 clear protocols and care pathways for these patients. If bedside staff notify the treating physician
206 or on-call resident instead of directly activating the stroke code, delayed notification is assured.
207 Another possible reason for delay could be erroneous attribution of stroke symptoms to non-
208 acute neurological symptoms triggering delayed general neurology consultations instead of direct
209 stroke team activation.¹ Furthermore, patient comorbidities and their post-surgical state may bias
210 staff towards prematurely concluding that stroke activation is futile or of little benefit. This only
211 underscores the importance of widespread education regarding the availability of effective non-
212 thrombolytic treatment options like mechanical thrombectomy, even in later time-windows,
213 which can reduce post-stroke morbidity and mortality.

214 *Stroke investigation and treatment*

215 Streamlined workflows with rapid access to baseline neurovascular imaging are essential in
216 effective acute stroke management. In our study, the median time from “first time seen
217 symptomatic” to imaging was not significantly different between in-hospital and out-of hospital
218 stroke groups. However, this represents suboptimal management of hospitalized strokes as these
219 patients are already physically closer to the imaging suite. Given the very short delays between
220 imaging and treatment initiation (i.e. time to administration of a bolus of intravenous
221 thrombolysis) in both groups (9 min in hospitalised and 11 min in out-of hospital strokes), our
222 results emphasize that time from symptom onset to imaging is where quality improvement

223 efforts should be focused for in-hospital strokes. Again, formal protocols detailing where
224 neurovascular imaging should be done for in-hospital strokes (ex. emergency department CT
225 versus radiology department CT) and where thrombolysis administration should occur (ex. CT
226 scan room, stroke unit, ICU, patient's own unit) can better inform hospital personnel and thereby
227 reduce uncertainty and unnecessary delays.

228 Only 57% of in-hospital patients were evaluated by the stroke team within 4.5 hours of the last
229 time seen well as compared to 74% of out-of hospital patients ($p = 0.03$). The significant
230 discrepancy ($p = 0.01$) between the proportion of patients who received thrombolysis in strokes
231 in hospitalized patients (12.8%) and out-of hospital strokes (45.4%) is likely only partially
232 explained by delayed evaluations. We found a similar discrepancy between patients who had
233 both thrombolysis and thrombectomy being 2.6% in the in-hospital group and 18.2% in the out-
234 of hospital (18.2%), ($p = 0.02$) stroke group. Given that 62.8% of hospitalized stroke patients had
235 a recent procedure or surgery prior to their stroke, IV thrombolysis is more likely to be contra-
236 indicated in this group. The difference in thrombolysis administration rates was not explained by
237 anticoagulant use, as the proportion of anticoagulated patients was similar in both groups.

238 *Potential solutions*

239 The management of in-hospital strokes could, in theory, be more rapid and streamlined, given
240 that the patient is already hospitalized and monitored by medical personnel. There is certainly an
241 unmet need for stroke awareness education among medical and non-medical staff. Recognition
242 of sudden-onset focal neurological deficits using simple tools like FAST, as well as regular
243 training to identify other stroke-like symptoms among patients with pre-existing co-morbidities,
244 should be offered to all clinical hospital staff caring for in-patients. Training should also focus on
245 nursing or medical staff notifying the stroke team using the stroke code as soon as there is a
246 suspicion of stroke, without notifying the general neurology team or general on-call resident
247 first. The development of an in-hospital stroke protocol can increase the efficiency of patient
248 management and treatment administration (see algorithm detailing standard of care for treatment
249 of in-hospital strokes at our center in Figure 2).²⁴ Indeed, having clear directions to follow makes
250 it easier for healthcare professionals to react within the therapeutic time window, thereby
251 reducing management delays and increasing the possibility for in-hospital stroke patients to have
252 access to appropriate acute stroke treatment.^{16,25-27} These need to be tailored to local
253 infrastructure, but should include clear delineation of the medical team responsible for evaluating

254 that patient (stroke physician, stroke nurse), having rapid access to thrombolytic therapy (ex. a
255 dedicated stroke toolbox for in-hospital strokes in a fixed, easily accessible location), ensuring
256 proper intravenous access and acute stroke laboratory tests, identifying patient transport
257 protocols and location of neurovascular imaging, determining where thrombolytic therapy will
258 be administered and where the patient will be admitted for specialized stroke care.
259 Implementation of regular stroke code activation simulations following detailed in-hospital
260 protocols may also contribute toward reducing false positive activations which can represent an
261 important burden on acute neurology services.

262 *Strengths*

263 A strength of this study is the inclusion of patients for which the stroke team was not notified, by
264 comparing patients identified by the medical archivists using ICD codes with data from the
265 electronic patient record that includes all acute stroke codes evaluated by the vascular neurology
266 team. Given that a large majority of these “missed” patients were post-operative, we identified an
267 area of unmet need wherein future quality improvement initiatives could be tailored to focus on
268 surgical and intensive care units. Another strength was the use of standardized data collection
269 tool among patients for whom the stroke team was activated, using a clinical report form
270 completed at the time of patient evaluation, allowing for more complete retrospective data
271 gathering.

272 *Limitations*

273 Our study has several limitations. The retrospective design is subject to many pitfalls and biases.
274 Our sample size was relatively small and captured from a single comprehensive stroke center,
275 with insufficient power to provide statistical significance when comparing both groups and
276 attenuating generalizability of our findings. Our results were heterogeneous, representing the
277 diversity of stroke cases encountered but also limiting the analysis and without adjustment for
278 potential confounding factors. The calculation of stroke metrics like time to imaging could be
279 influenced by variability in estimation of first onset of stroke symptoms in both groups. Our
280 study did not evaluate patients with false positive stroke code activations. Finally, we did not
281 have access to clinical outcomes beyond the index hospitalization period.

282 **Conclusion**

283 This study did not reveal significant differences between overall treatment time metrics in the
284 management of in-hospital compared to out-of hospital stroke patients. However, substantial

285 delays in stroke symptom recognition and stroke team activation were observed in patients with a
286 stroke while being hospitalised. Since these delays are likely modifiable, institutions should
287 emphasize targeted interventions to help expedite and expand treatment of in-hospital stroke
288 patients to potentially decrease hospital stays and post-stroke morbidity, such as systematic
289 hospital staff stroke recognition training and dedicated, widely circulated in-hospital acute stroke
290 protocols.

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