

1 **Patients' characteristics and outcomes depending on complete or incomplete**
2 **unilateral spatial neglect**

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23 **Abstract**

24 Unilateral spatial neglect (USN) is known to depress the activities of daily living. The
25 purpose of this study was to clarify that categorizing the type of USN using line
26 cancelation and line bisection tests is important when evaluating patients with acute
27 intracerebral hemorrhage (ICH). In this study, patients with ICH were prospectively
28 evaluated for the presence of USN using line cancelation and line bisection tests. They
29 were classified into an incomplete USN group (iUSN = abnormal results in either test) or
30 a complete USN group (cUSN = abnormal findings in both tests). We compared the
31 initial severity of ICH and the outcomes of USN in the two groups. We were able to
32 assess 16 patients, among whom 10 showed USN. Seven were then categorized as
33 having iUSN and three as having cUSN. The median hematoma volume was larger in
34 the cUSN group than in the iUSN group. The USN symptoms of patients in the iUSN
35 group disappeared during the chronic phase, whereas the symptoms of patients in the
36 cUSN group continued. The type of USN was associated with the initial severity of ICH
37 and the persistence of USN.

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39 **Keywords** Cerebral hemorrhage, acute • Unilateral spatial neglect • Rehabilitation •
40 Outcome • Line cancelation • Line bisection

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43 **Introduction**

44 Unilateral spatial neglect (USN) is a symptom defined as failure to report, respond, or
45 orient to contralateral stimuli that is not caused by an elemental sensorimotor deficit.
46 Although little is known about whether the frequency of USN associated with
47 hemorrhagic stroke is higher or lower than that with ischemic stroke, the age and sex of
48 the patient and the site and size of the lesion may influence the frequency of USN [1].
49 USN was demonstrated in 81.3 % of patients with right intracerebral hemorrhage (ICH)
50 in the subacute phase and was associated with diminished activities of daily living
51 (ADL) during the chronic phase [2-4].

52 Because of the disturbed consciousness and change in neurologic function, evaluation
53 of USN is difficult in the acute setting. In many studies, assessment for USN was
54 conducted about 1 month after the onset of stroke. Earlier evaluation may be helpful to
55 predict the presence of USN at discharge and the total length of hospital stay [5]. We
56 conjectured that simple evaluation using line cancellation and line bisection tests would
57 be meaningful for assessing patients with acute ICH. Importantly, it has not been
58 determined whether the severity of USN during the acute phase of stroke could predict
59 the severity of USN during the chronic phase. We hypothesized that the line cancellation
60 and line bisection tests could be used to confirm the presence of USN and that these
61 simple evaluations could identify an association between the initial severity of ICH and
62 the persistence of USN.

63

64 **Materials and methods**

65 Patients with putaminal or thalamic hemorrhage being treated at the Department of
66 Neurosurgery, Fukuoka University Hospital, Japan, were registered prospectively from
67 May 2012 to April 2014 to evaluate USN. Beginning from the start of their evaluation,
68 the total term of this study was May 2012 to April 2014. We intended for this
69 observational prospective study to last longer, but we had to cease registering patients in
70 April 2014 because of a shortage of speech therapists (STs). We included patients with
71 both right- and left-sided hemorrhagic stroke. Patients were excluded if they experienced
72 consciousness disturbance, aphasia, or significant visual disorder that interfered with
73 their ability to perform the USN evaluation. We did not exclude patients with motor
74 deficits because the method of evaluating USN was so easy that they could be checked
75 using the non-affected hand. The ethics committee of Fukuoka University Hospital

76 approved this study. Written informed consent was obtained from all patients or their
77 families.

78 A speech therapist (J.W.) evaluated USN using the line cancelation and line bisection
79 tests. The protocol for these tests has been described previously [2]. The patients were
80 diagnosed to have USN depending on whether they identified that more than 70 % of
81 uncrossed lines were on the same side as the brain lesion (line cancelation test) or the
82 marked point deviated more than 12.75 mm of the midpoint on the 204-mm line (line
83 bisection test). USN was confirmed based on the abnormality of either test. Patients with
84 abnormal results in either test were categorized as having incomplete USN (iUSN), and
85 those with abnormal findings in both tests were determined to have complete USN
86 (cUSN).

87 Patients' characteristics, region volume, and location of the hematoma as evaluated
88 by initial computed tomography (CT) were recorded at admission. The neurologic
89 symptoms were evaluated at the time of the USN examination. All study patients were
90 moved to a convalescence-stage hospital for further rehabilitation. The duration of
91 hospital stay and the presence or absence of USN at discharge were determined by
92 checking the clinical reports from the convalescence hospitals. USN at discharge from a
93 convalescence hospital was determined based on the Behavioral Inattention Test and/or
94 the Catherin Bergego scale [6].

95

96 **Statistical analysis**

97 Patients' background and hematoma characteristics were compared between the iUSN
98 and cUSN groups. The data of the patients gathered before leaving our hospital were
99 their age, sex, co-morbidities (hypertension, diabetes mellitus, smoking, drinking); the
100 affected side, site, and volume of the hematoma; Glasgow Coma Scale score; presence
101 of aphasia, paralysis, visual disorder; National Institutes of Health Stroke Scale/Score;
102 operation. The data collected before their leaving the convalescence hospital were the
103 presence of USN, total hospital stay, and modified Rankin Scale score. The frequency of
104 USN persistence and total hospital stay at the convalescence-stage hospital were
105 compared between groups.

106 Statistical significance of continuous variables was assessed using either
107 parametric or nonparametric tests, depending on whether the values were normally
108 distributed (analyzed with the Shapiro–Wilk test). Fisher's exact test was conducted to

109 assess the categorical variables. A value of $p < 0.05$ was considered to indicate statistical
110 significance. Data were analyzed using SPSS Version 22.0 (IBM Corp., Armonk, NY,
111 USA).

112

113 **Results**

114 Among the 40 patients who had either putaminal or thalamic hemorrhage, examination
115 for USN was incomplete in 24 because of disturbed consciousness ($n=16$), severe
116 attentional problem or aphasia ($n=5$), visual disability ($n=2$), or delirium ($n=1$) (Fig. 1).
117 The patients were assessed for USN at a median of 5 days from onset. USN was deemed
118 present in 10 patients. Thus, the 10 patients comprised the study group. The data from all
119 of them were complete. Seven were categorized as belonging in the iUSN group, and
120 three were deemed appropriate for the cUSN group (Table 1). No differences in the
121 frequency of USN were observed between right- and left-sided hemorrhage. Nor did the
122 frequency of a visual disorder differ between those with cUSN and iUSN.

123 The median hematoma volume was 61.8 mL in the cUSN group, which was
124 significantly greater than that in the iUSN group (10.2 mL) ($p = 0.017$, Mann–Whitney
125 U test). Patients in the cUSN group were evaluated on day 15, whereas the median day
126 of evaluation for the iUSN group was day 4 ($p = 0.057$, Mann–Whitney U test).
127 Significantly more severe neurologic symptoms were seen in more patients in the cUSN
128 group than in the iUSN group. Total hospital stay tended to be longer for the cUSN
129 group than the iUSN group. Whereas USN resolved in the iUSN group before discharge
130 from the convalescence hospital, it continued after discharge in the cUSN group.

131

132 **Discussion**

133 The hypothesis of this study was that the type of USN portended the initial severity of
134 ICH and the persistence of USN. We showed that the type of USN was significantly
135 associated with not only the characteristics of ICH but also the outcome of the USN
136 patients at discharge, proving our hypothesis.

137 Because USN sometimes constrains stroke patients from undergoing rehabilitation or
138 living at home, it is important to predict whether USN remains in the chronic phase.
139 Although there are many tests for USN that could provide a more precise diagnosis,
140 neurologic complications such as confusion, aphasia, apraxia, or paralysis frequently
141 interfere with the evaluation of USN. Maeshima et al. [2] reported that transient or

142 permanent USN was associated with the quantity of hematoma at admission and with the
143 Barthel index at discharge [1]. We proposed the utility of simple evaluations of USN
144 (line cancellation and line bisection tests), which showed significant association with the
145 characteristics in the acute stage and the outcome in the chronic stage. One of the
146 advantages of the method used in our study was its simplicity, which enabled us to
147 predict accurately the patients who would have persistent USN. This simple
148 categorization of iUSN and cUSN may predict the severity of the hematoma and the
149 outcome of USN in patients with ICH.

150 This study also indicated that the frequency of USN in the acute stage was not
151 significantly different between right- and left-sided hemorrhages, but there was a
152 difference depending on the volume of the hematoma. One possible explanation is that
153 deep nuclei and periventricular fibers are associated with the recognition of space
154 through the cortico-cortical fiber pathway, so USN can be easily seen in the deep brain
155 lesion [2].

156 There are some limitations in this study. First, the sample size was small, thereby
157 making the numbers of patients in each group small. Thus, a multiple regression analysis
158 could not be performed. Second, the hematoma volume was definitively larger in
159 patients with cUSN than in those with iUSN. Thus, it is possible that hematoma volume,
160 rather than USN type, was the main factor associated with USN persistence. Third, the
161 patients with iUSN might have had cUSN at admission. The timing of the evaluation
162 might have affected the results. Further studies are needed to evaluate this point. Fourth,
163 we diagnosed USN using the Behavioral Inattention Test and/or the Catherin Bergego
164 scale during the chronic phase. The Behavioral Inattention Test is used for the clinical
165 and objective diagnosis of USN, whereas the Catherine Bergego evaluates the impact of
166 USN on activities of daily living. However, it was left to the convalescence hospital
167 whether to use one or the other test, and thus we were unable to analyze those scores.
168 Another limitation was that the methods for evaluating line bisection and cancellation
169 differ greatly from the methods used in the Behavioral Inattention Test or Catherin
170 Bergego scale during the chronic phase. We did, however, demonstrate the usefulness of
171 these simple methods for evaluating USN in the acute setting.

172

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175 sponsor had no role in the design or conduct of this research.

176

177 **Conflicts of interest**

178 The authors declare that they have no conflict of interest.

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180 **Ethical approval**

181 All procedures performed in studies involving human participants were in accordance
182 with the ethical standards of the institutional research committee and with the 1964
183 Helsinki declaration and its later amendments or comparable ethical standards.

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185 **Informed consent**

186 Informed consent was obtained from all individual participants included in this study.

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191 **References**

- 192 1 Ringman JM, Saver JL, Woolson RF, Clarke WR, Adams HP: Frequency, risk
193 factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*.
194 2004;63:468-474.
- 195 2 Maeshima S, Ueyoshi A, Matsumoto T, Boh-oka S, Yoshida M, Itakura T, et al.:
196 Unilateral spatial neglect in patients with cerebral hemorrhage: The relationship between
197 hematoma volume and prognosis. *J Clin Neurosci*. 2002;9:544-548.
- 198 3 Oh-Park M, Hung C, Chen P, Barrett AM: Severity of spatial neglect during
199 acute inpatient rehabilitation predicts community mobility after stroke. *PM & R : the*
200 *journal of injury, function, and rehabilitation*. 2014;6:716-722.
- 201 4 Nijboer T, van de Port I, Schepers V, Post M, Visser-Meily A: Predicting
202 functional outcome after stroke: The influence of neglect on basic activities in daily
203 living. *Frontiers in human neuroscience*. 2013;7:182.
- 204 5 Umarova RM, Nitschke K, Kaller CP, Kloppel S, Beume L, Mader I, et al.:
205 Predictors and signatures of recovery from neglect in acute stroke. *Annals of neurology*.
206 2016;79:673-686.
- 207 6 Azouvi P, Olivier S, de Montety G, Samuel C, Louis-Dreyfus A, Tesio L:
208 Behavioral assessment of unilateral neglect: Study of the psychometric properties of the
209 catherine bergego scale. *Archives of physical medicine and rehabilitation*.
210 2003;84:51-57.

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213 **Table 1** Patients' characteristics and outcomes depending on complete or incomplete
 214 unilateral spatial neglect
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	complete (n=3)	Incomplete (n=7)	P value	DF
Age	59.7 ± 15.3	67.1 ± 8.4	0.33*	8.0
Sex (female)	3 (100%)	3 (42.9%)	0.20	
Hypertension	3 (100%)	6 (85.7%)	1.00	
Diabetes mellitus	0 (0%)	3 (42.9%)	0.48	
Smoking	0 (0%)	0 (0%)		
Drinking	0 (0%)	3 (42.9%)	0.48	
Side (right)	2 (66.7%)	4 (57.1%)	1.00	
Site of hematoma	thalamus 0 putamen 3	thalamus 5 putamen 2	0.17	
Volume of hematoma (ml)	61.8 (55.0-90.0)	10.2 (4.8-14.5)	0.017**	
GCS	10 (9-11)	15 (14-15)	0.017**	
Aphasia	1 (33.3%)	1 (14.3%)	1.00	
Paralysis	3 (100%)	6 (85.7%)	1.00	
Visual disorder	1 (33.3%)	1 (14.3%)	1.00	
NIHSS	20 (18-25)	11 (10-14)	0.033**	
Operation	3 (100%)	2 (28.6%)	0.17	
USN at discharge	3 (100%)	0 (0%)	0.008	
Total hospital stay (days)	232 ± 69	134 ± 67	0.068*	8.0
Modified Rankin Scale	4 (4-4)	3 (2-4)	0.12*	

216 The F and P value of Levene's test on age was 2.6 and 0.15 respectively.
217 The F and P value of Levene's test on total hospital staying was 0.01 and 0.92.
218 *Unpaired t-test, **Mann-Whitney U-test. NIHSS; National Institute of Health and Stroke
219 Scale, GCS; Glasgow Coma Scale. DF; degree of freedom

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224 **Figure legend**

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226

227 **Fig. 1** Patient enrollment for analysis based on the presence and types of unilateral

228 spatial neglect

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