

## Would intravitreal bevacizumab injection increase risk of cerebral infarction?

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### Purpose

There has been controversy concerning the possible association between intravitreal bevacizumab injection (IVB) injection and thromboembolic accidents. Some studies reported no association between IVB injection and stroke or myocardial infarction (MI). Several other studies have reported the possible association between IVB injection and thromboembolic accidents. The use of IVB for AMD has been increased with time for aged community. Thus, the relation between IVB and thromboembolic accidents should be uncovered. Although previous studies have investigated the effects of IVB injection on cerebral infarction, the effects of IVB are still not fully understood. The aim of this study was to determine the effects of IVB on cerebral infarction. In a small-scale study, we identified possible new risk factors, providing a basis for future population-based studies.

### Material and Methods

We retrospectively reviewed patients with AMD who received IVB injections for 1 year and determined the incidence of CI within 60 days after IVB injection to analyze the possible association between IVB and CI.

### Results

Over a 12-month period, 263 patients were enrolled. Six patients (2.28%) were diagnosed with CI within 2 months after receiving an IVB injection. The average number of IVB injections over the 1-year period was  $2.98 \pm 1.58$  and was not significantly different between the two groups. The total number of IVB injections per patient was  $4.95 \pm 3.31$  and was not significantly different between the two groups (Table 1). The incidence of CI in patients 75–84 years of age was 6.38%. These results showed a higher incidence of patients with IVB injections than the results of previous epidemiological studies (0.13% for all age groups, 1.68% for patients 75–84 years of age). All CI occurred 21–53 days after the IVB injection (mean:  $39.33 \pm 14.65$  days). Logistic regression analyses showed that age and a history of previous cerebral infarction were factors associated with cerebral infarction ( $p = 0.042$  and  $p = 0.008$ , respectively; Table 2). However, the total number of IVB injections and the number of IVB injections over 1 year were not associated with cerebral infarction (Table 2).

### Conclusions

Treatment with IVB may be an independent risk factor for cerebral infarction. Careful consideration by clinicians is necessary before administering IVB injections, especially in older patients or in patients with a previous history of cerebral infarction. These results are therefore useful for planning treatment strategies for patients with AMD, as well as for prevention of cerebral infarction.

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**Table 1. Demographic and baseline clinical characteristics of the patients**

	Non-cerebral infarction (n = 257)	Cerebral infarction (n = 6)	p-value
Age (years)	70.02 ± 11.69	80.33 ± 2.42	< 0.001
Sex (male:female)	144:113	4:2	0.699
Average IVB in a year	2.98 ± 1.59	2.83 ± 0.75	0.998
Total IVB number	4.90 ± 3.29	7.00 ± 4.10	0.091
History of cerebral infarction	10 (3.89%)	2 (33.3%)	0.026

IVB, intravitreal bevacizumab

**Table 2. Variables associated with cerebral infarction to IVB upon logistic regression analysis.**

	Univariate analysis		Stepwise regression analysis	
	$\beta \pm SE$	p value	$\beta \pm SE$	p value
Age (years)	0.112 ± 0.055	0.041	0.116 ± 0.057	0.042
sex	0.451 ± 0.875	0.607		
IVB during a year	-0.065 ± 0.278	0.816		
Total number of IVB	0.130 ± 0.088	0.140		
DM	0.366 ± 0.344	0.287		
Hypertension	18.976 ± 2197.245	0.993		
History of CI	2.514 ± 0.924	0.007	2.594 ± 0.984	0.008

IVB, intravitreal bevacizumab; DM, diabetes mellitus; CI, cerebral infarction