Do the Components of CHA₂DS₂-VAsc Score Affect Stroke Severity and Outcome?

Takeshi Hayashi, MD, PhD

Do the CHADS₂ and CHA₂DS₂-VAsc scores predict the prognosis of AF-associated ischemic stroke? This has long been controversial, but the answer is now emerging from obscurity – and it is “yes.”

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The CHADS₂ and CHA₂DS₂-VAsc scores are well-known stroke risk stratification tools for patients with AF. Whether these scores predict stroke outcome has been a matter of debate; Anegawa et al¹ reported that the CHADS₂ score was not related to the severity or outcome of stroke, and we found that these scores did not predict whether cardiogenic ischemic brain attack became permanent or not.² However, recent studies with larger numbers of patients revealed that these scores are useful for predicting stroke severity and prognosis (Table). We and others reported that patients with larger CHADS₂ scores showed worse functional outcomes.^{3–5} Large vessels, such as the internal carotid artery, tended to be occluded in such patients, indicating that the causative thrombus was larger.⁶ In-hospital mortality^{5,7} was also associated with CHADS₂ score.

In this issue of the Journal, Nezu et al⁸ show that initial neurological deficits were more severe in patients with larger CHA₂DS₂-VAsc scores. Because far more patients were enrolled in these studies than in previous ones,^{1,2} it is feasible to consider that the CHADS₂ and CHA₂DS₂-VAsc scores actually predict the severity and prognosis of AF-associated ischemic stroke.

Why then do these scores predict stroke prognosis? Because

the mechanisms of thrombus formation and growth are essentially the same. As shown in the Figure, each component of these scores (other than stroke history, vascular disease, and female sex) causes blood stasis, endothelial dysfunction, or hypercoagulability, all of which facilitate thrombus formation and consequent cerebral embolism. Likewise, each component of these scores (again, other than stroke history, vascular disease, and female sex) enhances thrombus growth, which makes the causative thrombus larger and resulting stroke more severe. Thus these scores are associated with both ischemic stroke occurrence and severity.

What about the role of female sex on stroke occurrence and severity (Figure)? Unlike other components, the mechanisms of the effect of female sex on thrombus formation and consequent stroke occurrence are unclear. Although studies from Western countries have revealed female sex as a stroke risk factor,⁹ the J-RHYTHM Registry showed that sex did not affect stroke risk in Japanese AF patients.¹⁰ Low body weight rather than female sex could be a risk for thromboembolism.¹¹ This is still a matter of debate. How female sex affects stroke prognosis is far more elusive. Experimental studies showed that male brains are more vulnerable to ischemic insults,^{12,13} which apparently conflicts with the result of the human study presented in this issue.⁸ As described,⁸ factors other than biological should be implicated: warfarin control, and familial or social support may differ. To elucidate the reasons for the difference in stroke prognosis between the sexes would give a clue to what we should do next in stroke medicine.

Table. Recent Reports That Investigated the Relationship of CHADS₂ Components With Stroke Severity and Outcome

	Functional outcome (mRS ≥3)			In-hospital mortality		Stroke severity (NIHSS)
	Deguchi et al ³	Tanaka et al ⁴	JSSRS 2015 ⁵	JSSRS 2015 ⁵	Yaghi et al ⁷	Nezu et al ⁸
	P value	P value	P value	P value	Odds ratio	β coefficient
Heart failure	0.073	<0.001	–	–	1.61	0.039
Hypertension	0.280	0.201	0.842	0.774	–	–
Age	<0.001	<0.001	<0.001	0.001	1.27	0.162
Diabetes mellitus	0.593	0.465	<0.001	<0.001	1.24	0.020
Stroke history	–	0.019	0.910	0.080	–	0.085

JSSRS, Japan Standard Stroke Registry Study; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale.

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Department of Neurology and Cerebrovascular Medicine, Saitama Medical University International Medical Center, Saitama, Japan

Mailing address: Takeshi Hayashi, MD, PhD, Department of Neurology and Cerebrovascular Medicine, Saitama Medical University

International Medical Center, Yamane 1397, Hidaka, Saitama 350-1298, Japan. E-mail: thayashi@saitama-med.ac.jp

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