LETTER TO THE EDITOR

Risk of Symptomatic Intracerebral Hemorrhage after Thrombolysis with rt-PA: The SEDAN Score

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The most feared complication after therapy with recombinant tissue plasminogen activator (rt-PA) in patients with acute ischemic stroke is the occurrence of symptomatic intracerebral hemorrhage (sICH). Up to 11% of stroke patients who undergo treatment with rt-PA have suffered from sICH, which in turn dramatically increases the in-hospital mortality rate as well as the functional disability [1–4].

Since 1996, when the US Food and Drug Administration approved thrombolysis with rt-PA for the treatment of patients with acute ischemic stroke, several different scores have been proposed to predict the risk of bleeding and outcomes, but none of them has been established in a clinical routine [4–7]. Strbian et al. [8] introduced a new score (SEDAN score).

The SEDAN score (0–6 points), which is based on blood sugar (glucose, 8.1–12.0 mmol/L [145–216 mg/dL] = 1, >12.0 mmol/L [216 mg/dL] = 2), early infarct signs (yes = 1), (hyper) dense cerebral artery sign (yes = 1) on computed tomography (CT) scan at admission, age (>75 years = 1), and National Institutes of Health Stroke Scale (NIHSS) score (≥ 10 = 1), has been suggested to predict the risk of sICH after IV thrombolysis. The rate of sICH ranged between 1% for 0 score points and 27.8% for 5 score points, with an area under curve (AUC) value of 0.77 (0.71–0.83) [8].

We included 542 stroke patients (mean age, 73 ± 13 years; 51% women; median NIHSS score, 11 [IQR, 7–15]) who were admitted to the Department of Neurology at the University of Lübeck from 2008 to 2013 and administered an IV treatment with rt-PA to validate the SEDAN score in a monocenter study. The data acquisition was a part of the stroke registry at the Department of Neurology at the University of Lübeck. All consecutive patients with AIS who were treated with rt-PA were included in our analysis. The baseline characteristics are shown in Table 1.

After the intravenous thrombolysis with 0.9 mg/kg of rt-PA, 50 of 542 patients (9.2%; 95% CI, 6.5–11.4%) suffered from sICH, as detected by follow-up CT scan. In our study, the SEDAN score was determined for 539 of 542 patients. Of these patients ($n = 539$), 11.7%, 28.0%, 28.2%, 19.3%, 10.0%, and 2.8% had 0, 1, 2, 3, 4, and ≥ 5 SEDAN points, respectively. The absolute risk of sICH was 0%, 4.6% (95% CI, 1.3–7.9%), 6.6% (95% CI, 3.3–10.5%), 13.5% (95% CI, 6.7–19.2%), 23.6% (95% CI, 12.7–34.5%), and 26.7% (95% CI, 12.7–34.5%) for 0, 1, 2, 3, 4, and ≥ 5 score points, respectively (Table 2). With increasing SEDAN score, the risk of sICH increased in the univariate analysis ($P < 0.001$). The logistic regression analysis showed that sICH was associated with increasing SEDAN score (OR, 1.93 per point; 95% CI, 1.51–2.46; $P < 0.001$). The predictive performance of the SEDAN score was assessed with the area under the receiver operating characteristic [AUC-ROC] (0.73; 95% CI, 0.65–0.80; $P < 0.001$).

The Hosmer–Lemeshow test revealed that the expected and observed rates of sICH among patients with and without sICH were 91.1% similar ($\chi^2 = 1.7$, $df = 3$, $P = 0.64$).

In the study, the majority of patients (87%) treated with IV thrombolysis had a SEDAN score of ≤ 3 points. Only 2.8% of patients had a SEDAN score of 5 or higher. Of the five factors that comprise the SEDAN score, the highest number of points was obtained from the NIHSS score at admission (NIHSS score ≥ 10 , 57.6%), followed by elderly age (44% of included patients >75 years old). The frequencies of infarct demarcation on CT scan at admission and of dense cerebral artery sign were 37.8% and 24.4%, respectively. However, an early infarct demarcation involving more than one-third of the area of the middle cerebral artery is a contraindication for treatment with IV thrombolysis.

Patients with higher SEDAN scores seem to be at a higher risk of suffering from sICH than those with lower SEDAN scores. Based on the SEDAN score, a concordance of 91.1% between expected

Table 1 A comparison between patients with versus without symptomatic intracerebral hemorrhage (sICH) after thrombolysis with rt-PA

sICH	Age, mean (SD)	Female sex	NIHSS score, median (IQR)	DTN, median	aHT	DM	HCH	Previous stroke	Atrial fibrillation
Yes (n = 50)	73 (13)	44%	16	58	82	34	16	32	48
No (n = 492)	72 (13) ^a	51 ^a	10 ^b	55 ^a	77 ^a	27 ^a	27 ^a	38 ^a	44 ^a

DTN, door to needle time; aHT, hypertension; DM, diabetes mellitus; HCH, hypercholesterolemia. Data are recorded in percentage unless otherwise indicated. ^aDifference: not significant. ^bDifference: significant.

Table 2 SEDAN score in all patients and in those suffering from sICH

SEDAN score	0	1	2	3	4	≥5
All patients (N = 539)	11.7	28.0	28.2	19.3	10.0	2.8
Risk of sICH	0	4.6	6.6	13.5	23.6	26.7

Data are recorded in percentage.

and observed sICH rates was found on the Hosmer–Lemeshow test.

An external validation of the SEDAN score among 34,251 patients enrolled in the ECASS II and Safe Implementation of Treatments in Stroke Monitoring Study (SITS-MOST) was retrospectively performed by Mazya et al. [9]. The predictive performance of the SEDAN score for sICH was moderate in ECASS II (AUC-ROC = 0.66) and low in SITS-MOST (AUC-ROC = 0.6). The difference between our findings and that of ECASS II and SITS-MOST could be caused by the difference in the cohort's size and the discrepancy of risk of hemorrhage. In the present study, the risk of sICH with 9.2% was comparable to the generally expected risk of hemorrhage (up to 10%),

whereas the frequency of sICH in SITS-MOST was remarkably low (1.8%) [9].

The predictive capability for sICH using SEDAN score with an AUC-ROC of 0.73 (95% CI, 0.65–0.80; $P < 0.001$) is comparable to the results of a recent prospective comparison of 6 scores estimating the risk of hemorrhage after thrombolysis. SEDAN was found to have the strongest predictive power (AUC-ROC, 0.7) [10].

However, the SEDAN score appears to be a valid tool for predicting the risk associated with the most severe type of complication: bleeding with clinical worsening. This finding may help physicians to focus attention on patients with higher SEDAN scores through attentive monitoring of vital parameters and intensive clinical evaluation during and after implementation of IV thrombolysis so as to prevent complications.

Conflict of Interest

The authors declare no conflict of interest.

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