Prior Use of Statins Improves Outcome in Patients With Intracerebral Hemorrhage
Prospective Data from the National Acute Stroke Israeli Surveys (NASIS)

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Background and Purpose—Intracerebral hemorrhage (ICH) is a deadly form of stroke. Pretreatment with statins exerts protective effects in patients with ischemic stroke, but their effects in patients with ICH remains unclear.

Methods—The National Acute Stroke Israeli Surveys (NASIS) included all patients admitted with acute stroke to any of the 28 hospitals nationwide during February through March 2003 and March through April 2007. We compared stroke severity and outcomes of ICH patients who received statins before the index event with those who did not, using multivariable logistic regression models adjusting for the propensity to use statins before the event.

Results—Among 3212 stroke patients, 312 had ICH and 89 of them were receiving statins at the time of the ICH. Patients on statins before ICH had lower baseline NIHSS scores, less systemic complications, higher proportions of good outcome (modified Rankin scale 0 to 3), lower death rates, and higher rates of discharge home or to a rehabilitation facility. On logistic regression analyses statin use before the event was associated with odds ratios of 0.46 for having a severe stroke defined as baseline NIHSS ≥15 (95% CI; 0.23 to 0.93), 2.97 for having good outcome (95% CI; 1.25 to 7.35) at discharge, and 0.25 for death or nursing facility disposition (95% CI; 0.09 to 0.63).

Conclusions—Use of statins before ICH is associated with reduced mortality and neurological disability and with a higher chance for good outcome, suggesting that statins may be protective in the setting of ICH. (Stroke. 2009; 40:2581-2584.)

Key Words: intracerebral hemorrhage ■ statins ■ neuroprotection ■ cholesterol
outcome. Because exact drug doses and length of treatment, LDL, and total cholesterol levels were not required for patients with ICH, these data were unavailable to us.

Statistical Methods
Differences in age-adjusted rates were compared using the Cochran-Mantel-Haenszel $\chi^2$ test. A propensity score estimating the likelihood of taking statins before ICH was calculated for each patient by logistic regression analysis that included 12 covariates. Multivariable logistic regressions were performed, adjusting for potential confounders and the propensity score of pre-ICH statin use stratified into terciles.

Results
Among the 3212 stroke patients included in NASIS 2003 and 2007, 312 (9.7%) fulfilled entry criteria for ICH, with a mean age of 77.4±9.9 years. Eighty-nine (28.5%) patients were reportedly on chronic statin therapy at the time of ICH onset. The demographic and risk factor profile of the patients are presented in Table 1.

At presentation to the hospital the neurological deficits were lower in patients that were on statins (Table 2). Furthermore, during hospitalization infectious complication rates were significantly lower for patients on statins as were death rates. In contrast, the chances for good outcome and discharge home or to a rehabilitation facility were higher in patients on statins. Of note, while the percentages of patients with excellent outcome (mRS 0 to 1) were similar between the 2 groups, the percentage of patients with good outcome (mRS 2 to 3) was much higher in patients treated with statins. Conversely, the percentage of patients with poor outcome (mRS 4 to 5) or death was much higher in untreated patients.

Multivariable logistic regression analyses adjusting for the propensity to receive statins (Table 3) revealed that pre-morbid statin use resulted in a more than 50% lower chance for having severe neurological deficits on admission (OR 0.46, 95% CI 0.23 to 0.93), a 3-fold increase in the chances of having a good outcome (OR 2.97, 95% CI 1.25 to 7.35), and a 75% lower chance of discharge to a chronic care nursing home or death (OR 0.25, 95% CI 0.09 to 0.63).

Discussion
The main findings of the current study are that the use of statins before ICH was associated with lower neurological disability at onset and a shift from poor to good outcome. This is also supported by the findings that significantly more patients on statins were discharged either home or to a rehabilitation facility.

Previous reports demonstrated induction of apoptosis, inflammation, and excitotoxic cascades after ICH, and statins may provide multi-faceted protective effects that could reduce such damage. However, findings regarding the
effects of statins in humans with ICH have been limited and inconclusive, with one study reporting protective effects and another failing to find such effects. Both studies were single-center retrospective analyses of data accrued over many years in contrast to the current prospective multi-center dataset. Furthermore, FitzMaurice and colleagues used different definitions of good outcome (GOS 4 to 5) at 90 days, which may account for the difference between the studies.

Importantly, in the prospective secondary prevention SPARC study, Atorvastatin treatment led to a slight increase in the frequency of cerebral hemorrhages. However, the study included only a few patients with ICH, and the exact effects of aggressive LDL lowering on the frequency of recurrent ICH remain unclear as previous studies failed to show an increase in the frequency of ICH.

Our study has several potential limitations. First, we recruited patients over 2 separate time windows in 2003 and 2007, but used similar methods and data acquisition forms. Second, because of the relatively small number of patients on statins before ICH we could not test whether statins before the ICH to reduce potential bias. Because of our limited statistical power and because our findings are novel, they should be regarded as hypothesis-generating and verified in other cohorts.

In conclusion, our study findings suggest that statins could have protective effects after ICH manifesting in reduced neurological deficits at presentation, lower death, and dependency rates and increased chances for good outcome.

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**Disclosures**

None.

**References**


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