

# Intracerebral hemorrhage recurrence

[Intracerebral hemorrhage](#) (ICH) is a disease with high mortality and a substantial risk of [recurrence](#) <sup>1</sup>.

However, the recurrence risk is poorly documented and the knowledge of potential predictors for recurrence among co-morbidities and medicine with [antithrombotic](#) effect is limited.

## Case series

### 2016

A [cohort](#) consisted of all individuals diagnosed with a primary ICH in [Denmark](#) 1996-2011. Information on comorbidities, surgical treatment for the primary ICH, and the use of ATT, SSRI's and NSAID's was retrieved from the Danish national health registers. The cumulative recurrence risk of ICH was estimated using the Aalen-Johansen estimator, thus taking into account the competing risk of death. Associations with potential predictors of recurrent ICH were estimated as rate ratios (RR's) using Poisson regression. Propensity score matching was used for the analyses of medicine with antithrombotic effects.

Among 15,270 individuals diagnosed with a primary ICH, 2,053 recurrences were recorded, resulting in cumulative recurrence risk of 8.9% after one year and 13.7% after five years. Surgical treatment and renal insufficiency were associated with increased recurrence risks (RR 1.64, 95% CI 1.39-1.93 and RR 1.72, 95% CI 1.34-2.17, respectively), whereas anti-hypertensive treatment was associated with a reduced risk (RR 0.82, 95% CI 0.74-0.91). We observed non-significant associations between the use of any of the investigated medicines with antithrombotic effect (ATT, SSRI's, NSAID's) and recurrent ICH.

The substantial short-and long-term recurrence risks warrant aggressive management of hypertension following a primary ICH, particularly in patients treated surgically for the primary ICH, and patients with renal insufficiency <sup>2</sup>.

### 2015

Single-site, tertiary care referral center observational study of 1145 of 2197 consecutive patients with ICH presenting from July 1994 to December 2013. A total of 1145 patients with ICH survived at least 90 days and were followed up through December 2013 (median follow-up of 36.8 months [minimum, 9.8 months]).

Blood pressure measurements at 3, 6, 9, and 12 months, and every 6 months thereafter, obtained from medical personnel (inpatient hospital or outpatient clinic medical or nursing staff) or via patient self-report. Exposure was characterized in 3 ways: (1) recorded systolic and diastolic measurements; (2) classification as adequate or inadequate BP control based on American Heart Association/American Stroke Association recommendations; and (3) stage of hypertension based on Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 7 criteria. MAIN OUTCOMES AND MEASURES: Recurrent ICH and its location within the brain (lobar vs nonlobar).

There were 102 recurrent ICH events among 505 survivors of lobar ICH and 44 recurrent ICH events among 640 survivors of nonlobar ICH. During follow-up adequate BP control was achieved on at least 1 measurement by 625 patients (54.6% of total [range, 49.2%-58.7%]) and consistently (ie, at all available time points) by 495 patients (43.2% of total [range, 34.5%-51.0%]). The event rate for lobar ICH was 84 per 1000 person-years among patients with inadequate BP control compared with 49 per 1000 person-years among patients with adequate BP control. For nonlobar ICH the event rate was 52 per 1000 person-years with inadequate BP control compared with 27 per 1000 person-years for patients with adequate BP control. In analyses modeling BP control as a time-varying variable, inadequate BP control was associated with higher risk of recurrence of both lobar ICH (hazard ratio [HR], 3.53 [95% CI, 1.65-7.54]) and nonlobar ICH (HR, 4.23 [95% CI, 1.02-17.52]). Systolic BP during follow-up was associated with increased risk of both lobar ICH recurrence (HR, 1.33 per 10-mm Hg increase [95% CI, 1.02-1.76]) and nonlobar ICH recurrence (HR, 1.54 [95% CI, 1.03-2.30]). Diastolic BP was associated with increased risk of nonlobar ICH recurrence (HR, 1.21 per 10-mm Hg increase [95% CI, 1.01-1.47]) but not with lobar ICH recurrence (HR, 1.36 [95% CI, 0.90-2.10]).

In this observational single-center cohort study of ICH survivors, reported BP measurements suggesting inadequate BP control during follow-up were associated with higher risk of both lobar and nonlobar ICH recurrence. These data suggest that randomized clinical trials are needed to address the benefits and risks of stricter BP control in ICH survivors <sup>3)</sup>.

## 2010

A total of 104 primary lobar ICH survivors were enrolled. Recurrence of lobar ICH was associated with previous ICH before index event (hazard ratio [HR] 7.7, 95% confidence interval [CI] 1.4-15.7), number of lobar microbleeds (HR 2.93 with 2-4 microbleeds present, 95% CI 1.3-4.0; HR = 4.12 when  $\geq 5$  microbleeds present, 95% CI 1.6-9.3), and presence of CT-defined white matter hypodensity in the posterior region (HR 4.11, 95% CI 1.01-12.2). Although aspirin after ICH was not associated with lobar ICH recurrence in univariate analyses, in multivariate analyses adjusting for baseline clinical predictors, it independently increased the risk of ICH recurrence (HR 3.95, 95% CI 1.6-8.3,  $p = 0.021$ ).

Recurrence of lobar ICH is associated with previous microbleeds or macrobleeds and posterior CT white matter hypodensity, which may be markers of severity for underlying cerebral amyloid angiopathy. Use of an antiplatelet agent following lobar ICH may also increase recurrence risk <sup>4)</sup>.

<sup>1)</sup> , <sup>4)</sup>

Biffi A, Halpin A, Towfighi A, Gilson A, Busl K, Rost N, Smith EE, Greenberg MS, Rosand J, Viswanathan A. Aspirin and recurrent intracerebral hemorrhage in cerebral amyloid angiopathy. *Neurology*. 2010 Aug 24;75(8):693-8. doi: 10.1212/WNL.0b013e3181eee40f. PubMed PMID: 20733144; PubMed Central PMCID: PMC2931649.

<sup>2)</sup>

Schmidt LB, Goertz S, Wohlfahrt J, Melbye M, Munch TN. Recurrent Intracerebral Hemorrhage: Associations with Comorbidities and Medicine with Antithrombotic Effects. *PLoS One*. 2016 Nov 10;11(11):e0166223. doi: 10.1371/journal.pone.0166223. PubMed PMID: 27832176.

<sup>3)</sup>

Biffi A, Anderson CD, Battey TW, Ayres AM, Greenberg SM, Viswanathan A, Rosand J. Association Between Blood Pressure Control and Risk of Recurrent Intracerebral Hemorrhage. *JAMA*. 2015 Sep 1;314(9):904-12. doi: 10.1001/jama.2015.10082. PubMed PMID: 26325559; PubMed Central PMCID: PMC4737594.

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