

## Is More Better? Using Metadata to Explore Dose–Response Relationships in Stroke Rehabilitation

Lohse and colleagues conducted a meta-analysis to investigate the relationship between therapy dose (time scheduled for therapy; hours) and change in motor function in adult patients after stroke. Studies that were not randomized, had >30% nonstroke patients, or that tested therapies in combination with a pharmaceutical treatment or electric stimulation were not considered. The main question was whether more therapy achieved better functional outcomes than less therapy. Standardized effect-sizes were calculated from the terminal difference between treatment and control or the difference in improvement between treatment and control. They controlled for the effect of years from initial stroke to the beginning of the intervention based on the hypothesis that delayed start after stroke may adversely affect outcome. Across the 34 included studies, there was a benefit for treatment groups receiving more therapy. The authors then conducted meta-regression analyses to quantify the dose–response relationship controlling for other factors in 30 studies with available data regarding the difference between groups in total time scheduled for therapy ( $\Delta$ Time;  $n=1750$  patients). The time poststroke was  $\approx 1.0 \pm 1.5$  years and the duration of therapy  $\approx 50 \pm 68$  days in both treatment and control groups. The average  $\Delta$ Time was  $33 \pm 36$  hours. Overall, increased  $\Delta$ Time was a significant predictor of increased improvement by itself and when controlling for linear and quadratic effects of time poststroke. Of note, the results suggested that the benefit of large increases in therapy is similar across a range of poststroke times regardless of whether a patient is several months or several years poststroke. Although the study cannot provide an answer to important questions such as how much is enough versus too much, it nevertheless highlights that increased practice improves outcome in a dose–response relationship, even at extended times poststroke. See p 2053.

## Acute Cerebrovascular Disease Occurring After Hospital Discharge for Labor and Delivery

Stroke is an uncommon but feared complication of pregnancy accounting for 5% to 14% of all maternal deaths. The highest risk is at the time of delivery to the postpartum period (6 weeks). However, there is a paucity of data regarding the incidence of stroke after discharge from the hospital as well as the associated risk factors. To elucidate these issues, Hovsepian and colleagues retrospectively analyzed data from California administrative claims databases. The primary outcome was acute cerebrovascular disease (CVD) as defined as hospitalization for ischemic stroke, intracerebral/subarachnoid/subdural/epidural hemorrhage, cerebral venous thrombosis, pituitary apoplexy, carotid/vertebral dissection, hypertensive encephalopathy, and other CVD. The secondary outcomes were ischemic stroke alone or intracerebral hemorrhage. Multivariable logistic regression was conducted to determine predictors for CVD including common pregnancy-related complications as well as traditional vascular risk factors, although the latter were rare in the studied population.

Overall, 2066230 patients were included in the analysis. Six-week CVD rates were 14.8/100000 patients (in-hospital mortality, 5.9%). The respective rates for ischemic stroke and intracerebral hemorrhage were 3.6/100000 (6.7% mortality) and 5.7/100000 (10.3% mortality), respectively. Risk factors for any CVD as well as ischemic stroke alone were preeclampsia, eclampsia, chronic kidney disease, black race, pregnancy-related hematologic disorders, and age. Preeclampsia, eclampsia, black race, and age were associated with an increased risk of intracerebral hemorrhage. These results indicate that the overall risk for postpartum stroke, although higher than in nonpregnant women, is low and largely associated with pregnancy-related complications. This study highlights that appropriate counseling of high-risk patients and their families is critical to raise awareness of this uncommon but potentially devastating complication to avoid delays in seeking medical attention. See p 1947.

## Cognitive Deterioration in Bilateral Asymptomatic Severe Carotid Stenosis

Buratti and colleagues present data regarding the cognitive performances in subjects with asymptomatic bilateral internal carotid artery stenosis  $\geq 70\%$  per Doppler criteria during a 3-year period. Baseline global cognitive function was evaluated by using the Mini Mental State Examination (MMSE) adjusted for age and education. Key exclusion criteria were age >85 years, disability (modified Rankin Scale score >0), documented or treated cognitive impairment, as well as poor temporal acoustic window or incompliance to cerebrovascular reactivity testing. Cerebrovascular reactivity to hypercapnia was quantified by the transcranial Doppler–based breath holding index (BHI) and the average of 3 tests included in the analysis. A BHI <0.69 was considered abnormal. The primary outcome was the difference in baseline versus 3-year follow-up MMSE. The analysis was performed on 159 subjects who completed the follow-up (patients with stroke or myocardial infarct during follow-up were excluded). Linear regression analyses indicated that hypertension, prior myocardial infarction, and left and right BHI were independently associated with follow-up MMSE. Furthermore, bilaterally pathological BHI were associated with higher MMSE score difference at 3 years as compared with unilateral abnormal BHI or bilaterally normal BHI, respectively. Of note, intima media thickness was not significantly associated with MMSE changes in this study. Important limitations of this study relate to the fact that no follow-up neuroimaging was obtained. This may have provided important insight into the progression of cerebral pathology such as silent infarcts or small-vessel disease–related sequelae. Furthermore, detailed cognitive assessment was not obtained, and details regarding chronic risk factor management and control are unknown. Thus, further study is needed to understand which patients are at highest risk for accelerated cognitive decline, the contribution of carotid stenosis, and, most importantly, the optimal therapeutic approach. Nevertheless, these results add to the notion that asymptomatic severe carotid stenosis may indeed be associated with chronic neurological consequences. See p 2072.

# Stroke

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