Acute Cerebrovascular Disease Occurring After Hospital Discharge for Labor and Delivery

Dominic A. Hovsepian, BS*; Nandita Sriram, BS*; Hooman Kamel, MD; Matthew E. Fink, MD; Babak B. Navi, MD

**Background and Purpose**—The risk of stroke and other postpartum cerebrovascular disease (CVD) occurring after hospital discharge for labor and delivery is uncertain.

**Methods**—We performed a retrospective cohort study using administrative databases to identify all pregnant women who were hospitalized for labor and delivery at nonfederal, acute care hospitals in California from 2005 to 2011 and who were discharged without an International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis of CVD. The primary outcome was an acute CVD composite defined as any ischemic stroke, intracranial hemorrhage, cerebral venous sinus thrombosis, pituitary apoplexy, carotid/vertebral artery dissection, hypertensive encephalopathy, or other acute CVD occurring after hospital discharge and before 6 weeks after labor and delivery. Descriptive statistics were used to estimate the incidence of postdischarge CVD. Multivariate logistic regression was used to evaluate the association between selected baseline factors and postdischarge CVD.

**Results**—The rate of any postdischarge acute CVD was 14.8 per 100 000 patients (95% confidence interval [CI], 13.2–16.5). Risk factors for any acute CVD were eclampsia (odds ratio [OR], 10.1; 95% CI, 3.09–32.8), chronic kidney disease (OR, 5.4; 95% CI, 2.5–11.8), black race (OR, 2.5; 95% CI, 1.9–3.3), preeclampsia (OR, 2.1; 95% CI, 1.6–2.8), pregnancy-related hematologic disorders (OR, 1.8; 95% CI, 1.3–2.5), and age (OR, 1.5 per decade; 95% CI, 1.3–1.8).

**Conclusions**—The incidence of postpartum acute CVD after hospital discharge for labor and delivery is similar to rates reported for all postpartum events in previous publications, suggesting that a substantial proportion of postpartum CVD occurs after discharge. *(Stroke. 2014;45:1947-1950.)*

**Key Words:** cerebral hemorrhage ■ postpartum period ■ pregnancy ■ stroke

**Methods**

**Study Design, Subjects, and Setting**

We conducted a retrospective cohort study using linked hospital discharge data from California administrative claims databases. The Office of Statewide Health Planning and Development, a division of the California Department of Health and Human Services, collects data on all emergency department visits and acute care hospital discharges at nonfederal health-care facilities throughout the state. These data undergo quality checks and are deidentified for use by the Agency for Healthcare Quality and Research for its Healthcare...
Cost and Utilization Project. Each patient in this database is given a unique record linkage number that allows for longitudinal tracking.

Using this database, we identified all pregnant women who were hospitalized for labor and delivery between January 1, 2005, and September 31, 2011, and discharged without any previous or concurrent International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis of CVD (430–438, 674.0, 671.5, 253.2, 443.21, and 443.24). Record linkage numbers were used to link subjects to any subsequent emergency department visit or hospitalization ≤6 weeks of labor and delivery. This study was certified as exempt from review by our institutional review board because our analysis was limited to publicly available deidentified data.

**Outcome Measurements**

The primary outcome was an acute CVD defined as any hospitalization for ischemic stroke (ICD-9-CM 433.x1, 434.x1, 436), intracerebral hemorrhage (431), subarachnoid hemorrhage (430), subdural or epidural hemorrhage (432), cerebral venous thrombosis (437.6, 671.5), pituitary apoplexy (253.2), carotid/vertebral artery dissection (443.21, 443.24), hypertensive encephalopathy (437.2), or other acute cerebrovascular disorders (437, 674.0). We included only events occurring after the initial hospital discharge and before 6 weeks after labor and delivery. However, in light of recent data demonstrating that the increased risk of postpartum thrombosis extends to ≤12 weeks, we also performed a post hoc analysis that included events occurring after the initial hospital discharge and before 12 weeks after labor and delivery. In addition, because pituitary apoplexy is not a typical cerebrovascular event, we performed a sensitivity analysis that excluded pituitary apoplexy from our primary outcome composite. Secondary outcomes were ischemic stroke alone or intracerebral hemorrhage alone, defined as any intracerebral, subarachnoid, subdural, or epidural hemorrhage during this same time period.

**Statistical Analysis**

Descriptive statistics with exact confidence intervals (CIs) were used to estimate the crude incidence of postpartum acute CVD after hospital discharge. Multivariate logistic regression was used to evaluate the association between postpartum acute CVD and the following a priori selected baseline factors: age, race, insurance status, pre-eclampsia (ICD-9-CM 642 except for 642.6), eclampsia (ICD-9-CM 642.6), peripartum hemorrhage (ICD-9-CM 666), peripartum infection (ICD-9-CM 659.2, 659.3, 670, 672), pregnancy-related hematologic disorders that consisted of primary hypercoagulable states and anemia and coagulation defects complicating pregnancy, childbirth, and delivery. In addition, because pituitary apoplexy is not a typical cerebrovascular event, we performed a sensitivity analysis that excluded pituitary apoplexy from our primary outcome composite. Secondary outcomes were ischemic stroke alone or intracerebral hemorrhage alone, defined as any intracerebral, subarachnoid, subdural, or epidural hemorrhage during this same time period.

**Results**

A total of 2 066 230 patients were included in the final analysis. Baseline patient characteristics, including demographic data and medical comorbidities, are outlined in Table 1. Notably, mean age was 28.3 (±6.5) years, and most patients were white (39.4%) or Hispanic (38.9%). Among the entire cohort, 8.4% had a comorbid diagnosis of a pregnancy-related hematologic disorder, 7.9% had preeclampsia, and 0.1% had eclampsia. Traditional vascular risk factors were rare in this population.

The primary outcome of any postpartum acute CVD occurring 6 weeks after hospital discharge for labor and delivery was diagnosed in 306 patients, which translates to a rate of 14.8 per 100 000 patients (95% CI, 13.2–16.5). The in-hospital mortality rate from any postdischarge acute CVD was 5.9% (95% CI, 3.2–8.5%). The mean age of patients with any postdischarge acute CVD was 30.2 years (95% CI, 29.5–30.9) as compared with 28.3 years (95% CI, 28.3–28.3) in patients without any postdischarge acute CVD (P<0.001).

Ischemic stroke alone was diagnosed in 75 patients, which translates to a rate of 3.6 per 100 000 patients (95% CI, 2.8–4.5). Intracranial hemorrhage alone was diagnosed in 117 patients, which translates to a rate of 5.7 per 100 000 patients (95% CI, 4.6–6.7). The in-hospital mortality rates for ischemic stroke and intracranial hemorrhage were 6.7% (95% CI, 0.9–12.4%) and 10.3% (95% CI, 4.7–15.8%), respectively.

Statistically significant risk factors for any acute CVD were eclampsia (odds ratio [OR], 10.1; 95% CI, 3.1–32.8), chronic kidney disease (OR, 5.4; 95% CI, 2.5–11.8), black race (OR, 2.5; 95% CI, 1.9–3.3), preeclampsia (OR, 2.1; 95% CI, 1.6–2.8), pregnancy-related hematologic disorders (OR, 1.8; 95%
CI, 1.2–2.5), and age (OR, 1.5 per decade; 95% CI, 1.3–1.8). There were nonsignificant but suggestive associations with several other baseline factors (Table 2).

Risk factors for ischemic stroke were eclampsia (OR, 12.9; 95% CI, 1.5–113.9), chronic kidney disease (OR, 4.7; 95% CI, 1.2–17.7), preeclampsia (OR, 3.7; 95% CI, 2.2–6.1), and black race (OR, 2.6; 95% CI, 1.4–4.8), pregnancy-related hematologic disorders (OR, 2.3; 95% CI, 1.3–3.9), and age (OR, 1.6 per decade; 95% CI, 1.1–2.1), whereas eclampsia (OR, 24.2; 95% CI, 6.0–97.2), black race (OR, 4.2; 95% CI, 2.5–7.1), preeclampsia (OR, 1.9; 95% CI, 1.2–3.0), and age (OR, 2.0 per decade; 95% CI, 1.4–2.7) were associated with an increased risk of intracranial hemorrhage.

In a post hoc analysis evaluating the incidence of acute CVD within the 12-week postpartum period, 356 patients were diagnosed with any postdischarge acute CVD among the 2066230 total patients, equating to a rate of 17.2 events per 100000 patients (95% CI, 15.4–19.0). The in-hospital mortality rate from any postdischarge acute CVD was 5.6% (95% CI, 3.2–8.0%). Ischemic stroke alone was diagnosed in 93 patients, which translates to a rate of 4.5 per 100000 patients (95% CI, 3.6–5.4). Intracranial hemorrhage alone was diagnosed in 137 patients, which translates to a rate of 6.6 per 100000 patients (95% CI, 5.5–7.7). The in-hospital mortality rates for ischemic stroke and intracranial hemorrhage were 5.4% (95% CI, 0.7–10.0%) and 10.2% (95% CI, 5.1–15.4%), respectively.

### Discussion

In a large and ethnically and socioeconomically diverse population, we found the incidence of postpartum acute CVD 6 weeks after hospital discharge for labor and delivery to be ≈15 per 100000 deliveries. Previous publications have reported the incidence of postpartum acute CVD to be anywhere from 8 to 22 per 100000 deliveries. Therefore, the incidence of postdischarge, postpartum acute CVD from our study falls within the range of incidences reported for all postpartum acute CVD. This suggests that a substantial proportion of postpartum cerebrovascular complications occur after hospital discharge.

| Table 2. Predictors of Postpartum Acute Cerebrovascular Disease After Hospital Discharge for Labor and Delivery* |
|--------------------------------------------------|-------------------|
| OR (95% CI)                                    | P Value |
| Edclampsias                                      | 10.1 (3.1–32.8)   | <0.001 |
| Chronic kidney disease                           | 5.4 (2.5–11.8)    | <0.001 |
| Black race                                       | 2.5 (1.9–3.3)     | <0.001 |
| Preeclampsia                                     | 2.1 (1.6–2.8)     | <0.001 |
| Pregnancy-related hematologic disorders           | 1.8 (1.2–2.5)     | 0.001  |
| Age, per decade                                  | 1.5 (1.3–1.8)     | <0.001 |
| Congestive heart failure                          | 3.4 (0.8–14.9)    | 0.110  |
| Peripartum infection                              | 2.5 (1.0–4.3)     | 0.052  |
| Diabetes mellitus                                 | 1.4 (1.0–2.0)     | 0.060  |

CI indicates confidence interval; and OR, odds ratio.

*A list of baseline clinical factors was selected a priori for inclusion in the model. Covariates that were not associated with the outcome at a significance level of P=0.20 were eliminated via stepwise reverse selection; the remaining covariates are shown here.

Few data exist regarding the incidence, mortality, and risk factors for acute CVD after hospital discharge for labor and delivery. One study examining data from 281000 deliveries recorded by the National Hospital Discharge Survey reported that postdischarge acute CVD accounted for 40% of all postpartum events. However, for a large proportion (36.5%) of pregnancy-related events in that study, the exact timing of the event (ie, antepartum, intrapartum, or postpartum) was unknown, and this may have skewed the true postdischarge event rate. In light of the fact that the average length of stay for labor and delivery is 2.6 days, our finding that a sizeable proportion of postpartum acute CVD occurs after hospital discharge is consistent with results from a previous study, which reported that the median onset of postpartum acute CVD is 8 days after delivery.

Previous studies have suggested that pregnancy itself may predispose to certain stroke risk factors, which could partly explain the increased stroke risk in the postpartum period. For instance, parity may slightly increase the risk of coronary heart disease. In addition, pregnancy is associated with increased serum cholesterol and triglyceride levels, which, although potentially adaptive to fetal–maternal needs, could theoretically increase the risk of atherosclerotic diseases. We found that eclampsia, preeclampsia, black race, chronic kidney disease, pregnancy-related hematologic disorders, and older age were independently associated with an increased risk of any postpartum acute CVD after hospital discharge. These risk factors are intuitive and consistent with those previously reported for all pregnancy-related acute CVD. Of note, the absolute rate of eclampsia was low in our study population, which may have been because of aggressive management of preeclampsia with magnesium sulfate administration. However, the relative risk of any postdischarge acute CVD in patients with eclampsia was increased >10-fold. This increased risk may partly be explained by the fact that eclampsia can manifest with posterior reversible encephalopathy syndrome, which is often interpreted or diagnosed as an acute CVD. In addition, hypertension, which is part of the eclampsia syndrome and a major risk factor for posterior reversible encephalopathy syndrome, has been found in multiple previous studies to be a significant risk factor for postpartum acute CVD. Although we cannot establish a causal relationship between postdischarge acute CVD and the risk factors we identified, these risk factors may be helpful in identifying patients at high risk of CVD after discharge who may potentially benefit from close monitoring and targeted efforts at risk factor modification.

In our secondary outcome analysis, we found that hemorrhagic strokes are more common than ischemic strokes after hospital discharge, which is consistent with results for all postpartum events in previous studies. The mortality rate from our study for postdischarge hemorrhagic events was ≈1.5 times greater than that for ischemic events, which is also supported by previous literature comparing pregnancy-related ischemic and hemorrhagic strokes. Several risk factors, including eclampsia, preeclampsia, black race, and older age, were common to both ischemic and hemorrhagic postdischarge acute CVD. However, chronic kidney disease and hematologic disorders were additional risk factors for postpartum ischemic strokes after hospital discharge, which may indicate mechanistic differences between these events.
The limitations of our study include the dependence on administrative data, which may have resulted in inaccuracies in diagnostic coding or misclassification of patients. Many of the ICD-9-CM codes used to identify risk factors and outcomes in this study have not been validated, which could have led to incorrect associations between comorbidities and postpartum acute CVD. However, similar associations in previous literature suggest that some correlation does exist between postdischarge acute CVD and the risk factors examined in our study. We also did not use data from federal healthcare facilities, which make up 3.1% of California facilities, but it is unlikely that the lack of data from this small percentage of facilities would have changed our numbers significantly. Finally, although our study contained a large number of postpartum women, the absolute rate of acute CVD was low, so our analysis of potential risk factors may have been underpowered, particularly for our subgroup analyses.

Previous work has shown that pregnancy confers a 3-fold increased risk of stroke compared with the nonpregnant state, and that the postpartum state is associated with an even higher risk. For instance, in a large cross-sectional study involving several dozens of New England hospitals, the relative risk of stroke during pregnancy and the 6-week postpartum period was 2.4, whereas the relative risk during the 6-week postpartum period alone was 7.9. Therefore, it is important for neurologists, obstetricians, and primary care physicians to be mindful of the incidence of acute CVD during the postpartum period. Our study expands on this message by demonstrating that many postpartum strokes occur after hospital discharge, when women are monitored less frequently and may be less cognizant of potential postpartum complications. The predominance of hemorrhagic strokes, coupled with their higher mortality rates, makes the consequences of these events even more clinically relevant. Clinicians should be aware that postpartum women remain at risk for stroke even if they have been discharged from their initial labor and delivery hospitalization without complication.

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Disclosures
Dr Kamel serves on the speaker’s bureau and consultant/advisory board for Genentech; this disclosed relationship is considered modest. Dr Fink serves as the Editor for Neurology Alert; this disclosed relationship is considered modest. The other authors report no conflicts.

References
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卒中存活者的体能锻炼推荐

American Heart Association/American Stroke Association

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

卒中后体能运动缺乏十分普遍。评估的大量证据明确支持卒中存活者的运动训练(有氧训练及力量性训练)是有用的。体能锻炼可提高存活者身体功能能力,日常生活能力和生活质量,并且降低了随后心血管事件的风险。卒中存活者的体能锻炼目标和规划需要个体化并尽可能地

方法:

写作团队的成员由美国心脏协会卒中理事会科学声明监督委员会和美国心脏协会审稿监督委员会任命。作者使用系统文献综述,参考已发表的研究结果进行研究,收集和评估研究,并撰写与卒中相关的体能锻炼的声明。该声明是基于现行的科学证据,并且不包含任何医学治疗的建议。

结论

卒中存活者的体能锻炼推荐

卒中及其他急性脑血管疾病(AVD)是我们所关心的急诊发生


利用这个数据集,我们确认了所有2005年1月1日至2011年9月31日期间因分娩住院的所有妊娠女性,且出院诊断中没有按照国际疾病分类修订第九版(COD-ICD-9-CM)定义的任何CVD。编码的可以使用与产后急性CVD诊断相关的分娩后12周内的任何住院的和非住院的事件。本研究是一个回顾性队列研究。研究结果是基于可获取的行政数据库。该研究被认证为可免除我们伦理审查委员会的审查,因为该分析受限于公开可用的数据库。

背景及目的:

我们使用行政数据库进行了一项回顾性队列研究以确定从2005年至2011年在加利福尼亚非联邦急诊医院因分娩住院的所有孕妇,且出院诊断中没有按照国际疾病分类修订第九版(COD-ICD-9-CM)定义的任何CVD。编码的可以使用与产后急性CVD诊断相关的分娩后12周内的任何住院的和非住院的事件。本研究是一个回顾性队列研究。研究结果是基于可获取的行政数据库。该研究被认证为可免除我们伦理审查委员会的审查,因为该分析受限于公开可用的数据库。

结果测定

主要结局是急性CVD定义为任何住院治疗的缺血性卒中,蛛网膜下腔出血,脑出血;产后期;怀孕;卒中


统计分析

我们使用这项研究在加利福尼亚非联邦急诊医院发生的卒中包括无症状卒中患者。我们使用ICD-9-CM编码来识别这些就诊。这些编码包括任何诊断编码为卒中,蛛网膜下腔出血,脑出血,或脑静脉血栓形成。我们的主要终点是任何住院治疗的缺血性卒中和颅内出血。次级终点包括蛛网膜下腔出血,脑出血,脑静脉血栓形成,以及任何住院的急性脑血管疾病。使用SPSS 17.1软件进行统计分析。我们使用描述性统计来估计出院后产后急性CVD的发生率。计数数据用χ2检验来评价治疗的选择与产后急性CVD的相关性。使用多元逻辑回归分析来评价治疗的选择与产后急性CVD的相关性。

卒中及其他急性脑血管疾病(AVD)是我们所关心的急诊发生


统计分析

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吸烟和酗酒。这些基线因素包括常见的妊娠并发症，均在本次分析中显现。妊娠相关的血液疾病（OR, 1.8; 95% CI, 1.2–2.5), 子痫前期 (OR, 2.1; 95% CI, 1.6–2.8), 黑人种族(OR, 2.5; 95% CI, 1.9–3.3), 子痫前期 (OR, 2.1; 95% CI, 1.6–2.8)。在评价产后 12 周内妊娠相关性 CVD 发生的研究中发现，2002230 例妊娠中有 36 例患者发生了妊娠 CVD，其中妊娠晚期发病率是 30.2/10 万 (95% CI, 25.9–35.0), 无元为妊娠期 CVD, 患者平均年龄为 28.3 (95% CI, 26.3–28.3) 岁, <0.001, 对照组 (除其他临床因素外) 进行了调整。急性 CVD 的发生率是 14.0/10 万, 无显著差异。<p>在共有 48 例的患者中有 75 例, 发生率是 3.6/10 万(95% CI, 3.2-8.0%)。诊断为缺血性卒中的患者有 93 例, 相当于十万分之 17.2(95% CI,15.4-19.0)。 产后急性 CVD 的院内死亡率为 5.6%(95% CI,4.7-8.2%)。另外还有 5%的患者种族信息未得到确认。这些人群中传统的血管危险因素比较罕见。年</p>