Original Research

Timing and Risk Factors of Postpartum Stroke

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OBJECTIVE: To characterize risk and timing of postpartum stroke readmission after delivery hospitalization discharge.

METHODS: The Healthcare Cost and Utilization Project's Nationwide Readmissions Database for calendar years 2013 and 2014 was used to perform a retrospective cohort study evaluating risk of readmission for stroke within 60 days of discharge from a delivery hospitalization. Risk was characterized as odds ratios (ORs) with 95% CIs based on whether patients had hypertensive diseases of pregnancy (gestational hypertension or preeclampsia), or chronic hypertension, or neither disorder during the index hospitalization. Adjusted models for stroke readmission risk were created.

RESULTS: From January 1, 2013, to October 31, 2013, and January 1, 2014, to October 31, 2014, 6,272,136 delivery hospitalizations were included in the analysis. One thousand five hundred five cases of readmission for postpartum stroke were identified. Two hundred fourteen (14.2%) cases of stroke occurred among patients with hypertensive diseases of pregnancy, 66 (4.4%) with chronic hypertension, and 1,225 (81.4%) without hypertension. The majority of stroke readmissions occurred within 10 days of hospital discharge (58.4%), including 53.2% of patients with hypertensive diseases of pregnancy during the index hospitalization, 66.7% with chronic hypertension, and 58.9% with no hypertension. Hypertensive diseases of pregnancy and chronic hypertension were associated with increased risk of stroke readmission compared with no hypertension (OR 1.74, 95% CI 1.33–2.27 and OR 1.88, 95% CI 1.19–2.96, respectively). Median times to readmission were 8.9 days for hypertensive diseases of pregnancy, 7.8 days for chronic hypertension, and 8.3 days without either condition.

CONCLUSION: Although patients with chronic hypertension and hypertensive diseases of pregnancy are at higher risk of postpartum stroke, they account for a minority of such strokes. The majority of readmissions for postpartum stroke occur within 10 days of discharge; optimal blood pressure management may be particularly important during this period.

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Pregnancy-associated stroke is a rare event with an incidence of approximately 34 per 100,000 deliveries.[1] However, the incidence may be increasing, particularly during the postpartum period. Analysis of nationally representative administrative data by the Centers for Disease Control and Prevention (CDC) found that in the United States, postpartum admissions for pregnancy-associated stroke increased 83% from 1994–1995 to 2006–2007.[2] Increased risk of pregnancy-associated stroke may be secondary in part to the increasing prevalence of hypertensive disorders.[2,3] Both chronic hypertension and hypertensive diseases of pregnancy including gestational hypertension and preeclampsia have been demonstrated to increase risk of pregnancy-associated stroke in epidemiologic studies.[1–4]

Severe-range blood pressure (BP) in pregnant or postpartum patients, and in particular systolic BP of 160 mm Hg or higher, may be associated with pregnancy-associated stroke.[5] The American College of Obstetricians and Gynecologists' Task Force on

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Hypertension in Pregnancy supports monitoring patients with hypertensive diseases of pregnancy for at least 72 hours postpartum and then again 7–10 days after delivery or earlier if symptoms are present.[6] For patients with systolic BP 150 mm Hg or diastolic BP 100 mm Hg, initiation of an antihypertensive agent is recommended.[6]

Improved BP management for patients with hypertensive diseases of pregnancy may reduce maternal risk from stroke.[7] However, research characterizing time intervals between delivery hospitalization discharge and readmission for acute stroke is limited.[8–10] Improved knowledge of timing of postpartum stroke may be helpful in optimizing postdischarge surveillance for high-risk patients. We sought to better characterize the time interval from delivery hospitalization discharge to stroke readmission for patients with and without diagnoses of hypertensive diseases of pregnancy and chronic hypertension as well as characterize risk factors for these events.

MATERIALS AND METHODS

The Healthcare Cost and Utilization Project's Nationwide Readmissions Database from 2013 and 2014 was used to perform this retrospective cohort study. The Nationwide Readmissions Database is an all-payer database collected on a state level that can be used to track patients across hospital admissions within a state, generating national estimates of readmissions for the insured and uninsured. The Nationwide Readmissions Database includes public hospitals, community hospitals, and academic medical centers[11] and has been used across a wide number of medical and surgical subspecialties to evaluate readmission hospitalizations.[12,13] The Nationwide Readmissions Database is part of the Healthcare Cost and Utilization Project that is sponsored by the Agency for Healthcare Research and Quality. The Healthcare Cost and Utilization Project State Inpatient Databases from which the Nationwide Readmissions Database is drawn contain reliable, verified patient linkage numbers while adhering to strict privacy guidelines.[11] Data in the Nationwide Readmissions Database is weighted to provide national estimates with an estimated 35 million U.S. discharges. In 2014, 22 geographically dispersed states contributed data to the Nationwide Readmissions Database, accounting for 51% of U.S. residents and 49% of all U.S. hospitalizations. The Columbia University and University of Southern California institutional review boards granted exemptions given that the Nationwide Readmissions Database is deidentified and publically available.

For this analysis, index delivery hospitalizations were captured with International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes 650 and V27.x. These criteria ascertain greater than 95% of delivery hospitalizations.[14] Females aged 15–54 years were included. The primary outcome of the analysis was a stroke readmission after a delivery hospitalization. The CDC severe maternal morbidity ICD-9-CM coding algorithm for puerperal cerebrovascular disorders was used to identify patients.[15] We included pregnancy-associated stroke readmission based on CDC criteria up to 60 days after discharge from a delivery hospitalization; we extended the analysis beyond 6 weeks postpartum to determine whether there was prolonged risk after delivery hospitalization. Women were classified into three groups based on diagnoses during the delivery hospitalization: 1) chronic hypertension without superimposed preeclampsia (ICD-9-CM 401.x, 402.x, 403.x, 404.x, 405.x, 642.0x, 642.1x, 642.2x); 2) hypertensive diseases of pregnancy (gestational hypertension, preeclampsia, severe preeclampsia, superimposed preeclampsia; ICD-9-CM 642.3x, 642.4x, 642.5x, and 642.7x, respectively); or 3) neither condition. To avoid misclassification of an historical compared with acute diagnosis, patients with a diagnosis of stroke during the delivery index hospitalization were excluded. To create national estimates, population weights from the Nationwide Readmissions Database were applied. Because the Nationwide Readmissions Database data sets are year-based and cannot be linked, only delivery hospitalizations where discharge occurred from January 1 through October 31 for each year were included; delivery hospitalizations during November and December were not included because readmissions for the subsequent 60 days could not be fully ascertained.

Demographic factors included maternal age, payer, and ZIP code income quartile. Risk factors included tobacco use, migraine headaches, pregestational diabetes, cesarean delivery during the index hospitalization, and maternal cardiovascular disorders including valvular, ischemic, and congenital disease. Hospital stays for delivery hospitalizations were dichotomized into longer and shorter stays; longer hospital stay was defined as greater than 4 days for cesarean delivery and greater than 3 days for vaginal delivery. Hospital factors included hospital bed size, teaching compared with nonteaching status, and location based on the National Center for Health Statistics Urban-Rural Classification Scheme for Counties.[16] To account for the influence of clinical and demographic factors on stroke, we used logistic regression models to estimate odds ratios (ORs) of factors associated with stroke readmission with 95% CIs.

In addition to the primary analysis described previously, we performed two sensitivity analyses. First, because administrative data are used primarily for billing purposes and misclassification is a concern with all analyses, we performed an analysis restricted to ICD-9-CM codes for stroke with high sensitivity ascertained in nonobstetric validation studies (430, 431, 434.x1, and 436) as well as ICD-9-CM code 674.0, which we have found to be highly sensitive in pregnancy-related stroke in our institution.[17–20] Second, because risk factors for hemorrhagic and occlusive stroke may differ, we performed analyses individually for these outcomes (intracerebral hemorrhage, ICD-9-CM 431; occlusive stroke ICD-9-CM 433.x, 434.x). For both sensitivity analyses, we repeated the univariate and adjusted analyses as well as reevaluated the temporal distribution of readmission events after delivery hospitalization discharge. Finally, in addition to these analyses, we determined 1) the proportion of patients with stroke readmission diagnosed with hypertensive diseases of pregnancy on readmission but not during the index hospitalization; and 2) risk of stroke individually for patients with superimposed preeclampsia, mild preeclampsia, severe preeclampsia, and gestational hypertension. All analyses were performed with SAS 9.4.

RESULTS

From January 1, 2013, to October 31, 2013, and January 1, 2014, to October 31, 2014, 6,272,136 delivery hospitalizations occurred and were included in the analysis. Based on CDC severe morbidity criteria, there were 1,505 cases of stroke (24.0/100,000 deliveries, 95% CI 22.8–25.2) that occurred within 60 days after a delivery hospitalization. Of these, 214 (14.2%, 95% 12.5–16.%) occurred in patients with hypertensive diseases of pregnancy, 66 (4.4%, 95% CI 3.4–5.5%) occurred in patients with chronic hypertension without superimposed preeclampsia, and 1,225 (81.4%, 95% CI 79.3–83.3%) occurred in patients without hypertension (Table 1).

Risk of postpartum stroke readmission within 60 days was 41.7 (95% CI 36.2–47.3) per 100,000 deliveries for patients with hypertensive diseases of pregnancy, 59.6 (95% CI 45.1–73.8) per 100,000 for patients with chronic hypertension without superimposed preeclampsia, and 21.7 (95% CI 20.5–22.9) per 100,000 for patients without either condition. The majority of stroke readmissions (58.4%) occurred within 10 days of hospital discharge including 53.2% of patients with hypertensive diseases of pregnancy during the index hospitalization, 66.7% with chronic hypertension without superimposed preeclampsia, and 58.9% with no hypertension (Fig. 1). The next 20-day period (postdischarge days 11–30) accounted for 31.3% of stroke readmissions associated with hypertensive diseases of pregnancy, 16.7% of readmissions associated with chronic hypertension, and 29.7% of stroke readmissions associated with neither diagnosis. The final 30 days accounted for 15.4% of stroke diagnoses associated with hypertensive diseases of pregnancy, 16.7% associated with chronic hypertension without superimposed preeclampsia, and 11.3% associated with neither diagnosis. Median times to readmission were 8.9 days for patients with hypertensive diseases of pregnancy (95% CI 6.4–11.4 days), 7.8 days for those with chronic hypertension without superimposed preeclampsia (95% CI 5.9–9.7 days), and 8.3 days for patients without either condition (95% CI 7.6–9.0 days). When a sensitivity analysis was restricted to ICD-9-CM codes 430, 431, 434.x1, 436, and 674.0x (n=1,043), the distribution of time to readmission was similar with the majority of readmissions (63.8%) occurring 1–10 days after discharge.

Women with either hypertensive diseases of pregnancy or chronic hypertension without superimposed preeclampsia were at increased risk of stroke readmission compared with patients without these conditions (OR 1.74, 95% CI 1.33–2.27 and OR 1.88, 95% CI 1.19–2.96, respectively) (Table 2). Women aged older than 39 years were at increased risk of stroke (OR 2.69, 95% CI 1.79–4.05) and patients aged 15–19 years were at decreased risk of stroke (OR 0.50, 95% CI 0.31–0.78) with maternal age 25–29 years as a reference. Other risk factors associated with maternal stroke included longer length of stay during the delivery hospitalization (OR 1.47, 95% CI 1.26–1.71), cesarean delivery (OR 1.28, 95% CI 1.07–1.51), pregestational diabetes (OR 1.70, 95% CI 1.04–2.78), tobacco use (OR 1.81, 95% CI 1.37–2.40), and Medicaid insurance (OR 1.65, OR 95% CI 1.35–2.03) with private insurance as a reference. Maternal cardiac disease, hospital teaching status and bed size, and ZIP code income quartile were not significantly associated with stroke readmission risk. When this analysis was restricted to higher sensitivity codes for stroke (ICD-9-CM codes 430, 431, 434.x1, 436, 674.0), similar ORs were noted (results not shown).

For the sensitivity analyses, 927 patients diagnosed with stroke had a high-sensitivity diagnostic code, 342 patients had an occlusive stroke, and 320 patients had an intracerebral hemorrhage. Results from the high-sensitivity adjusted analysis were similar to the primary analysis with chronic hypertension,

Table 1. Demographic, Medical, and Hospital Factors Associated With Postpartum Stroke Readmission

Factor	Stroke Readmission	No Stroke Readmission	*P*
All patients	1,505 (100)	6,270,631 (100)	
Hypertension			<.01
HDP	214 (14.2)	512,457 (8.2)	
Chronic hypertension	66 (4.4)	110,955 (1.8)	
None	1,225 (81.4)	5,647,218 (90.1)	
Age (y)			<.01
15–19	55 (3.7)	430,442 (6.9)	
20–24	246 (16.3)	1,393,780 (22.2)	
25–29	407 (27.0)	1,787,708 (28.5)	
30–34	426 (28.3)	1,688,886 (26.9)	
35–39	260 (17.2)	784,456 (12.5)	
Older than 39	112 (7.5)	185,358 (3.0)	
ZIP code income quartile			<.01
Lowest	460 (30.6)	1,648,410 (26.3)	
Low	402 (26.7)	1,623,536 (25.9)	
High	354 (23.5)	1,555,966 (24.8)	
Highest	278 (18.4)	1,383,436 (22.1)	
Data missing	12 (0.8)	59,282 (1.0)	
Insurance status			<.01
Medicare	13 (0.9)	40,652 (0.7)	
Medicaid	783 (52.0)	2,649,276 (42.3)	
Private	645 (42.8)	3,263,074 (52.2)	
Self-pay	24 (1.6)	99,962 (1.6)	
No charge	0 (0.0)	3,948 (0.1)	
Other	41 (2.7)	199,831 (3.2)	
Missing data	0 (0.0)	13,887 (0.2)	
Migraine	29 (1.9)	51,275 (0.8)	<.01
Maternal cardiac disease	8 (0.5)	18,985 (0.3)	.10
Tobacco	156 (10.5)	342,517 (5.5)	<.01
Pregestational diabetes	43 (2.9)	64,129 (1.0)	<.01
Cesarean delivery	628 (41.7)	2,034,336 (32.4)	<.01
Longer length of stay[†]	446 (29.6)	1,415,760 (22.6)	<.01
Hospital teaching			<.01
Metropolitan nonteaching	465 (30.9)	1,981,594 (31.6)	
Metropolitan teaching	913 (60.7)	3,634,728 (58.0)	
Nonmetropolitan	127 (8.5)	654,307 (10.4)	
Hospital location*			.02
Large central metropolitan counties	451 (30.0)	1,830,861 (29.2)	
Large fringe metropolitan counties	396 (26.3)	1,598,579 (25.5)	
Medium metropolitan counties	285 (18.9)	1,318,757 (21.1)	
Small metropolitan counties	187 (12.4)	609,081 (9.7)	
Micropolitan (less than 50,000 population)	115 (7.6)	538,255 (8.6)	
Not metro- or micropolitan	72 (4.8)	366,991 (5.9)	
Missing data	0 (0.0)	8,106 (0.1)	
Hospital bed size[‡]			.02
Small	170 (11.3)	836,292 (13.3)	
Medium	435 (28.9)	1,752,213 (27.9)	
Large	901 (59.8)	3,682,125 (58.7)	

HDP, hypertensive diseases of pregnancy.

Data are n (%) unless otherwise specified.

* As defined by the National Center for Health Statistics Urban-Rural Classification Scheme for Counties: large central metropolitan counties are metropolitan statistical areas (MSA) of 1 million or greater or more population that 1) contain the entire population of the largest principal city of the MSA; or 2) are completely contained in the largest principal city of the MSA; or 3) contain at least 250,000 residents of any principal city of the MSA. Large fringe metropolitan counties are counties in MSAs of 1 million or more population that do not qualify as large central. Medium metropolitan counties are counties in MSAs of 250,000–999,999 population. Small metropolitan counties are counties in MSAs of less than 250,000 population. From: https://www.cdc.gov/nchs/data_access/urban_rural.htm.

† Longer length of stay, greater than 4 days for cesarean delivery and greater than 3 days for vaginal delivery.

‡ Bed size classification is defined using number of beds, region of the United States, the urban–rural designation of the hospital in addition to the teaching status.

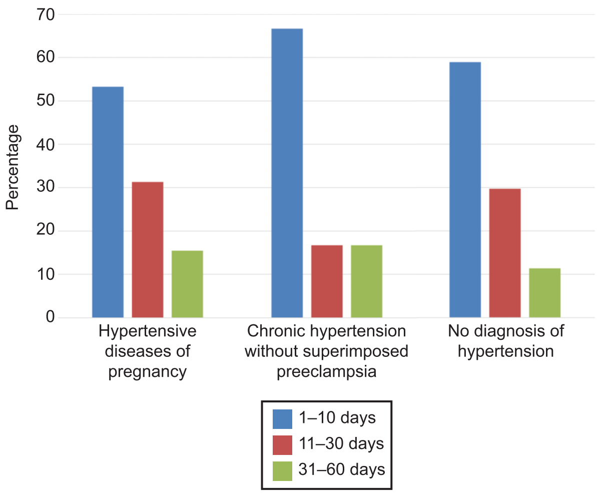

Fig. 1. The histogram demonstrates the proportion of stroke readmissions by hypertensive diagnosis over the first 60 days after hospital discharge. Hypertensive diseases of pregnancy include superimposed, severe, and mild or unspecified preeclampsia and gestational hypertension.

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hypertensive diseases of pregnancy, older maternal age, migraine headache, and tobacco use associated with increased risk of stroke (Table 3). For hemorrhagic stroke, factors associated with increased risk included maternal age older than 39 years and Medicaid insurance. Factors associated with increased risk of ischemic stroke included hypertensive diseases of pregnancy, maternal age older than 29 years, tobacco use, pregestational diabetes, and longer hospital stay. For patients readmitted within 60 days of a delivery hospitalization, 70.7% of readmissions for intracerebral hemorrhage occurred within the first 10 days after discharge.

Risk of postpartum stroke differed by specific hypertensive diseases of pregnancy diagnosis with risk highest for preeclampsia superimposed on chronic hypertension (72.0/100,000 deliveries, n=30) compared with severe preeclampsia (67.9/100,000 deliveries, n=70), mild preeclampsia (46.0/100,000 deliveries, n=63), and gestational hypertension (22.5/100,000, n=52). Overall, 27.3% of patients with chronic hypertensive (n=18) and 19.6% (n=239) of patients without chronic hypertension who did not have a hypertensive diseases of pregnancy diagnosis during the index delivery hospitalization had a hypertensive diseases of pregnancy diagnosis during readmission for postpartum stroke.

DISCUSSION

Pregnancy-associated stroke is an important cause of severe maternal morbidity and mortality and the postpartum period is associated with increased risk of this outcome with many events occurring after discharge home from a delivery hospitalization.[1,19,21] Although multiple risk factors for postpartum stroke have been identified in the literature, including hypertensive and other medical and obstetric conditions,[1] these data from a nationally representative sample suggest that postpartum strokes often occur soon after delivery.[5,21] Although postpartum stroke is relatively rare and the degree to which these events are preventable is unknown, these findings support prompt optimal BP management and evaluation of patients with concerning symptoms (such as unremitting headache and focal neurologic abnormalities) in the days immediately after hospital discharge.

Our data demonstrate the challenging nature of reducing risk of postpartum stroke readmission because more than 80% of patients readmitted with pregnancy-associated stroke did not have a diagnosis of hypertensive diseases of pregnancy or chronic hypertension during their index hospitalization. In the adjusted analyses, specific factors were associated with increased risk of pregnancy-associated stroke, but the magnitude of risk did not facilitate identification of a small, particularly high-risk cohort. Further research is required to characterize which patients may be at highest risk for events and determine what, if any, interventions may improve outcomes. Providing routine neurologic precautions at delivery discharge may represent a means of improving early detection of events. The use of mobile health technology strategies including text messaging and wireless device applications may represent a cost-effective means of patient monitoring and is an important focus for future research.[22–24] Large maternal safety collaboratives such as the California Maternal Quality Care Collaborative and New York State's Safe Motherhood Initiative may be able to further characterize which symptoms are most likely to be associated with pregnancy-associated stroke events.

The mechanism by which risk of stroke is increased postpartum is unknown but may be secondary to BP elevation that peaks 3–5 days after delivery secondary to fluid shifts along with impaired cerebral autoregulation.[25,26] Regardless of etiology, stroke risk is likely to continue to rise given that many risk factors such as older maternal age, pregestational diabetes, chronic hypertension, and other stroke-related high-risk conditions continue to increase on a population basis. Although further research is indicated to determine what mechanisms predispose patients to pregnancy-associated stroke, research on clinical interventions to reduce risk is needed now.

Table 2. Adjusted and Unadjusted Odds of Factors Associated With Postpartum Stroke Readmission

	Unadjusted Analysis		Adjusted Analysis	
	OR	95% CI	Adjusted OR	95% CI
Hypertension				
HDP	1.86	1.61–2.15	1.74	1.33–2.27
Chronic hypertension	2.55	1.99–3.26	1.88	1.19–2.96
None	0.48	0.42–0.55	1.00	Reference
Age (y)				
15–19	0.52	0.39–0.67	0.50	0.31–0.78
20–24	0.68	0.60–0.78	0.70	0.54–0.89
25–29	0.93	0.83–1.04	1.00	Reference
30–34	1.07	0.96–1.20	1.22	0.96–1.55
35–39	1.46	1.28–1.67	1.57	1.22–2.02
Older than 39	2.64	2.18–3.20	2.69	1.79–4.05
ZIP code income quartile				
Lowest	1.23	1.11–1.38	1.36	1.00–1.86
Low	1.04	0.93–1.17	1.25	0.91–1.70
High	0.93	0.83–1.05	1.15	0.84–1.57
Highest	0.80	0.70–0.91	1.00	Reference
Insurance status				
Medicare	1.34	0.77–2.31	1.22	0.53–2.84
Medicaid	1.48	1.34–1.64	1.65	1.35–2.03
Private	0.69	0.62–0.77	1.00	Reference
Self-pay	1.00	0.67–1.50	1.28	0.69–2.37
Other	0.85	0.62–1.16	1.14	0.70–1.84
Migraine	2.38	1.65–3.44	2.08	1.00–4.32
Maternal cardiac disease	1.76	0.88–3.53	1.31	0.48–3.57
Pregestational diabetes	2.85	2.10–3.86	1.70	1.04–2.78
Cesarean delivery	1.49	1.35–1.65	1.28	1.07–1.51
Tobacco	2.00	1.70–2.36	1.81	1.37–2.40
Longer length of stay	1.44	1.29–1.61	1.47	1.26–1.71
Hospital teaching				
Metropolitan nonteaching	0.97	0.87–1.08	1.00	Reference
Metropolitan teaching	1.12	1.01–1.24	1.05	0.86–1.27
Nonmetropolitan	0.79	0.66–0.95	0.86	0.51–1.48
Hospital location*				
Large central metropolitan counties	1.04	0.93–1.16	1.00	Reference
Large fringe metropolitan counties	1.04	0.93–1.17	1.11	0.88–1.40
Medium metropolitan counties	0.88	0.77–0.99	0.93	0.74–1.18
Small metropolitan counties	1.32	1.13–1.54	1.33	0.99–1.80
Micropolitan (less than 50,000 population)	0.88	0.73–1.07	0.99	0.58–1.69
Not metro- or micropolitan	0.81	0.64–1.03	0.88	0.51–1.52
Hospital bed size†				
Small	0.83	0.71–0.97	1.00	Reference
Medium	1.05	0.94–1.17	1.21	0.87–1.67
Large	1.05	0.95–1.16	1.17	0.87–1.56

OR, odds ratio; HDP, hypertensive diseases of pregnancy.

The adjusted model included all the covariates listed in the table's CI. Longer length of stay, greater than 4 days for cesarean delivery and greater than 3 days for vaginal delivery.

* As defined by the National Center for Health Statistics Urban-Rural Classification Scheme for Counties: large central metropolitan counties are metropolitan statistical areas (MSA) of 1 million or greater or more population that 1) contain the entire population of the largest principal city of the MSA; or 2) are completely contained in the largest principal city of the MSA; or 3) contain at least 250,000 residents of any principal city of the MSA. Large fringe metropolitan counties are counties in MSAs of 1 million or more population that do not qualify as large central. Medium metropolitan counties are counties in MSAs of 250,000–999,999 population. Small metropolitan counties are counties in MSAs of less than 250,000 population. From: https://www.cdc.gov/nchs/data_access/urban_rural.htm.

† Bed size classification is defined using number of beds, region of the United States, the urban–rural designation of the hospital in addition to the teaching status.

Strengths of this study include a large nationally representative sample designed to analyze hospital readmissions, allowing a detailed adjusted analysis for this rare outcome. The validity of our findings on the temporal distribution of readmissions was enhanced by the fact that both the primary and the sensitivity

Table 3. Sensitivity Analyses

	High-Sensitivity Codes	Hemorrhagic Stroke	Ischemic Stroke
Hypertension			
HDP	1.53 (1.06–2.21)	1.02 (0.56–1.86)	2.36 (1.40–3.97)
Chronic hypertension	1.88 (1.07–3.30)	1.54 (0.64–3.68)	1.56 (0.47–5.14)
None	1.00 (reference)	1.00 (reference)	1.00 (reference)
Age (y)			
15–19	0.23 (0.10–0.51)	0.16 (0.04–0.64)	0.41 (0.11–1.49)
20–24	0.64 (0.46–0.89)	0.73 (0.45–1.19)	0.90 (0.49–1.63)
25–29	1.00 (reference)	1.00 (reference)	1.00 (reference)
30–34	1.36 (1.01–1.82)	1.05 (0.65–1.68)	2.18 (1.33–3.58)
35–39	1.90 (1.39–2.60)	1.16 (0.68–1.99)	2.49 (1.48–4.17)
Older than 39	3.56 (2.14–5.91)	3.81 (1.86–7.80)	3.97 (1.75–9.02)
ZIP code income quartile			
Lowest	1.62 (1.15–2.28)	1.28 (0.78–2.12)	1.45 (0.82–2.57)
Low	1.29 (0.91–1.83)	1.41 (0.81–2.46)	1.26 (0.73–2.19)
High	1.06 (0.75–1.50)	0.78 (0.45–1.33)	1.27 (0.66–2.05)
Highest	1.00 (reference)	1.00 (reference)	1.00 (reference)
Insurance status			
Medicare	0.53 (1.13–2.17)	NA	1.26 (0.30–5.24)
Medicaid	1.42 (1.12–1.80)	1.50 (1.01–2.23)	1.27 (0.88–1.82)
Private	1.00 (reference)	1.00 (reference)	1.00 (reference)
Self-pay	1.10 (0.52–2.32)	1.93 (0.72–5.16)	0.33 (0.05–2.37)
Other	0.86 (0.43–1.73)	1.62 (0.69–3.81)	0.63 (0.15–2.67)
Migraine	2.50 (1.01–6.20)	1.23 (0.29–5.13)	2.34 (0.49–11.22)
Maternal cardiac disease	0.99 (0.24–4.14)	1.46 (0.21–10.22)	2.47 (0.59–10.35)
Tobacco	2.30 (1.63–3.26)	1.75 (0.92–3.34)	2.24 (1.26–3.98)
Pregestational diabetes	1.40 (0.72–2.71)	0.34 (0.05–2.49)	2.46 (1.09–5.54)
Cesarean delivery	1.11 (0.88–1.41)	1.13 (0.76–1.68)	1.42 (0.95–2.12)
Longer length of stay*	1.27 (0.98–1.65)	1.31 (0.89–1.92)	1.55 (1.02–2.36)
Hospital teaching			
Metropolitan nonteaching	1.00 (reference)	1.00 (reference)	1.00 (reference)
Metropolitan teaching	0.93 (0.73–1.19)	0.99 (0.67–1.44)	1.06 (0.71–1.57)
Nonmetropolitan	0.70 (0.36–1.37)	0.71 (0.16–3.14)	1.55 (0.49–4.84)
Hospital location†			
Large central metropolitan counties	1.00 (reference)	1.00 (reference)	1.00 (reference)
Large fringe metropolitan counties	1.18 (0.89–1.56)	0.95 (0.61–1.49)	1.17 (0.73–1.86)
Medium metropolitan counties	0.99 (0.73–1.51)	0.96 (0.58–1.57)	1.00 (0.62–1.61)
Small metropolitan counties	1.01 (0.67–1.51)	0.78 (0.40–1.51)	1.03 (0.57–1.87)
Micropolitan (less than 50,000 population)	1.00 (0.53–1.89)	0.50 (0.13–1.88)	0.46 (0.12–70)
Not metro- or micropolitan	0.77 (0.38–1.54)	0.09 (0.01–0.89)	0.67 (0.25–1.79)
Hospital bed size‡			
Small	1.00 (reference)	1.00 (reference)	1.00 (reference)
Medium	0.96 (0.65–1.42)	0.85 (0.46–1.56)	1.09 (0.55–2.14)
Large	0.96 (0.67–1.39)	1.07 (0.60–1.89)	0.93 (0.51–1.69)

HDP, hypertensive diseases of pregnancy.
Data are adjusted odds ratio (95% CI).
* Longer length of stay, greater than 4 days for cesarean delivery and greater than 3 days for vaginal delivery.
† As defined by the National Center for Health Statistics Urban-Rural Classification Scheme for Counties: large central metropolitan counties are metropolitan statistical areas (MSA) of 1 million or greater or more population that 1) contain the entire population of the largest principal city of the MSA; or 2) are completely contained in the largest principal city of the MSA; or 3) contain at least 250,000 residents of any principal city of the MSA. Large fringe metropolitan counties are counties in MSAs of 1 million or more population that do not qualify as large central. Medium metropolitan counties are counties in MSAs of 250,000–999,999 population. Small metropolitan counties are counties in MSAs of less than 250,000 population. From: https://www.cdc.gov/nchs/data_access/urban_rural.htm.
‡ Bed size classification is defined using number of beds, region of the United States, the urban–rural designation of the hospital in addition to the teaching status.

analyses demonstrated similar results as did analysis of specific hypertensive diseases of pregnancy diagnoses. Although misclassification and underascertainment are always concerns with administrative diagnosis codes, the sensitivity analysis restricted to higher sensitivity codes[20] demonstrated similar results to the primary model in the univariate and adjusted analyses. Other factors that enhance the strength of the analysis include that codes for hypertensive diseases of pregnancy are relatively sensitive,[16,27,28] and that to avoid misclassification between historical and acute events, we excluded patients with diagnoses of pregnancy-associated stroke during the index admission. Finally, the approach to identifying stroke in administrative data is the same as that utilized by the CDC, and prevalence of this condition was similar to readmission risk ascertained in their analysis of data from the Nationwide Inpatient Sample.[2,29]

Limitations of the study include shortcomings inherent to administrative data, which provide a broad overview of population-based risk, but lack many important clinical details. Although we were able to stratify patients based on specific preeclampsia diagnoses, we were unable to examine the severity of disease, BP control, and interventions that were performed such as use of antihypertensive or antithrombotic medications. Additionally, administrative data do not capture important risk factors such as body mass index that may modify risk, and many secondary diagnoses are likely underascertained. Discharge medication administration, including initiation of estrogen-containing birth control, was not available. Another limitation is that from this database we were not able to model the interval from date of delivery to stroke readmission and used discharge date instead. Additionally, because some stroke codes including those that are pregnancy-related are not specific with regard to the event being hemorrhagic or ischemic, only a minority of the events in our cohort was able be evaluated in our sensitivity analysis limiting powering. Finally, although we adjusted for variables such as payer and median income, which are related to race, we were not able to account for race directly because this variable is not included in the data set.

In conclusion, although this analysis found that risk of stroke was associated with conditions such as hypertensive diseases of pregnancy and chronic hypertension, the most important risk factor was time from discharge with most readmissions occurring within the first 10 days home from the hospital. This temporal relationship may be important in designing safety interventions for at-risk patients, and the relatively short period may represent an opportunity to meaningfully improve maternal outcomes.

REFERENCES

1. James AH, Bushnell CD, Jamison MG, Myers ER. Incidence and risk factors for stroke in pregnancy and the puerperium. Obstet Gynecol 2005;106:509–16.
2. Kuklina EV, Tong X, Bansil P, George MG, Callaghan WM. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: reasons for concern? Stroke 2011;42:2564–70.
3. Leffert LR, Clancy CR, Bateman BT, Bryant AS, Kuklina EV. Hypertensive disorders and pregnancy-related stroke: frequency, trends, risk factors, and outcomes. Obstet Gynecol 2015;125:124–31.
4. Scott CA, Bewley S, Rudd A, Spark P, Kurinczuk JJ, Brocklehurst P, et al. Incidence, risk factors, management, and outcomes of stroke in pregnancy. Obstet Gynecol 2012;120:318–24.
5. Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. Obstet Gynecol 2005;105:246–54.
6. Executive summary: hypertension in Pregnancy. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:1122–31.
7. Clark SL, Christmas JT, Frye DR, Meyers JA, Perlin JB. Maternal mortality in the United States: predictability and the impact of protocols on fatal postcesarean pulmonary embolism and hypertension-related intracranial hemorrhage. Am J Obstet Gynecol 2014;211:32.e1–9.
8. Witlin AG, Mattar F, Sibai BM. Postpartum stroke: a twenty-year experience. Am J Obstet Gynecol 2000;183:83–8.
9. Salonen Ros H, Lichtenstein P, Bellocco R, Petersson G, Cnattingius S. Increased risks of circulatory diseases in late pregnancy and puerperium. Epidemiology 2001;12:456–60.
10. Tate J, Bushnell C. Pregnancy and stroke risk in women. Womens Health (Lond) 2011;7:363–74.
11. Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project. Introduction to the HCUP Nationwide Readmissions Database: 2014. April 2017. https://www.hcup-us.ahrq.gov/db/nation/nrd/Introduction_NRD_2010-2014.pdf. Retrieved November 1, 2017.
12. Kurtz SM, Lau EC, Ong KL, Adler EM, Kolisek FR, Manley MT. Which clinical and patient factors influence the national economic burden of hospital readmissions after total joint arthroplasty? Clin Orthop Relat Res 2017 Jan. 20 [Epub ahead of print].
13. Poojary P, Saha A, Chauhan K, Simoes P, Sands BE, Cho J, et al. Predictors of hospital readmissions for ulcerative colitis in the United States: a national database study. Inflamm Bowel Dis 2017;23:347–356.
14. Kuklina E, Whiteman M, Hillis S, Jameieson D, Meikle S, Posner S, et al. An enhanced method for identifying obstetric deliveries: implications for estimating maternal morbidity. Matern Child Health J 2008;12:469–77.
15. Centers for Disease Control and Prevention. Severe Maternal Morbidity. Available at: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/severematernalmorbidity.html. Retrieved March 1, 2017.
16. The National Center for Health Statistics. The NCHS Urban-Rural Classification Scheme for Counties. Available at: https://www.cdc.gov/nchs/data_access/urban_rural.htm. Retrieved August 20, 2017.
17. Jones SA, Gottesman RF, Shahar E, Wruck L, Rosamond WD. Validity of hospital discharge diagnosis codes for stroke: the Atherosclerosis Risk in Communities Study. Stroke 2014;45:3219–25.
18. Roumie CL, Mitchel E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiol Drug Saf 2008;17:20–6.

19. Miller EC, Gatollari HJ, Too G, Boehme AK, Leffert L, Elkind MS, et al. Risk of pregnancy-associated stroke across age groups in New York state. JAMA Neurol 2016;73:1461–7.
20. McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. PLoS One 2015;10:e0135834.
21. Kittner SJ, Stern BJ, Feeser BR, Hebel R, Nagey DA, Buchholz DW, et al. Pregnancy and the risk of stroke. N Engl J Med 1996;335:768–74.
22. Rehman H, Kamal AK, Morris PB, Sayani S, Merchant AT, Virani SS. Mobile health (mHealth) technology for the management of hypertension and hyperlipidemia: slow start but loads of potential. Curr Atheroscler Rep 2017;19:12.
23. Vodopivec-Jamsek V, de Jongh T, Gurol-Urganci I, Atun R, Car J. Mobile phone messaging for preventive health care. The Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD007457. DOI: 10.1002/14651858.CD007457.pub2.
24. Willcox JC, Wilkinson SA, Lappas M, Ball K, Crawford D, McCarthy EA, et al. A mobile health intervention promoting healthy gestational weight gain for women entering pregnancy at a high body mass index: the txt4two pilot randomised controlled trial. BJOG 2017;24:1718–28.
25. Magee L, von Dadelszen P. Prevention and treatment of postpartum hypertension. The Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD004351. DOI: 10.1002/14651858.CD004351.pub3.
26. van Veen TR, Panerai RB, Haeri S, Griffioen AC, Zeeman GG, Belfort MA. Cerebral autoregulation in normal pregnancy and preeclampsia. Obstet Gynecol 2013;122:1064–9.
27. Yasmeen S, Romano PS, Schembri ME, Keyzer JM, Gilbert WM. Accuracy of obstetric diagnoses and procedures in hospital discharge data. Am J Obstet Gynecol 2006;194:992–1001.
28. Palmsten K, Huybrechts KF, Kowal MK, Mogun H, Hernández-Díaz S. Validity of maternal and infant outcomes within nationwide Medicaid data. Pharmacoepidemiol Drug Saf 2014;23:646–55.
29. Callaghan WM, Creanga AA, Kuklina EV. Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. Obstet Gynecol 2012;120:1029–36.