Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management during Pregnancy

Consensus Statement

Hemorrhagic Stroke

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STROKE IN PREGNANCY Writing Group and the
Canadian Stroke Best Practices and Quality Advisory Committees,
in collaboration with the Canadian Stroke Consortium

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Published Guidelines

Guideline	Recommendations
Frontera JA, Lewin III JJ, Rabinstein AA, Aisiku IP, Alexandrov AW, Cook AM, Del Zoppo GJ, Kumar MA, Peerschke EI, Stiefel MF, Teitelbaum JS. **Guideline for Reversal of Antithrombotics in Intracranial Hemorrhage** **A Statement for Healthcare Professionals from the Neurocritical Care Society and Society of Critical Care Medicine** ***Neurocritical care.* 2016;24(1):6-46.**	No guideline statement specific to pregnancy
Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, Fung GL, Goldstein JN, Macdonald RL, Mitchell PH, Scott PA, Selim MH, Woo D; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, and Council on Clinical Cardiology. **Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2015;46:2032–2060.**	No guideline statements specific to pregnancy
Steiner T, Al-Shahi Salman R, Beer R, et al. **European Stroke Organisation (ESO) guidelines for the management of spontaneous intracerebral**	No guideline statements specific to pregnancy

Guideline	Recommendations
haemorrhage. ***Int J Stroke 2014*;9:840–855.**	
Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G: **European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage.** ***Cerebrovasc Dis 2013*;35:93-112.**	No guideline statements specific to pregnancy
E. Sander Connolly, Jr, Alejandro A. Rabinstein, J. Ricardo Carhuapoma, Colin P. Derdeyn, Jacques Dion, Randall T. Higashida, Brian L. Hoh, Catherine J. Kirkness, Andrew M. Naidech, Christopher S. Ogilvy, Aman B. Patel, B. Gregory Thompson, and Paul Vespa , on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Radiology and Intervention, Council on Cardiovascular Nursing, Council on Cardiovascular Surgery and Anesthesia, and Council on Clinical Cardiology **Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association** ***Stroke 2012*; 43: 1711–1737.**	No guideline statements specific to pregnancy
Diringer MN, Bleck TP, Claude HJ, III, Menon D, Shutter L, Vespa P, Bruder N, Connolly ES, Jr., Citerio G, Gress D, Hanggi D, Hoh BL, Lanzino G, Le RP,	No guideline statements specific to pregnancy

Guideline	Recommendations
Rabinstein A, Schmutzhard E, Stocchetti N, Suarez JI, Treggiari M, Tseng MY, Vergouwen MD, Wolf S, Zipfel G: **Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference.** ***Neurocrit Care 2011*;15:211-240.**	

Evidence Tables

Incidence of Hemorrhagic Stroke

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kuklina et al. 2011 **USA** **Retrospective study**	All pregnant-related hospitalizations from 1994-1997.	Comparison of trends in pregnancy-related stroke between 1994-1995 and 2006-2007 were examined using data obtained from the Nationwide Inpatient Sample, a nationally representative database which sampled 20% of all discharges.	Rates of stroke (ischemic, hemorrhagic, ICH, SAH, TIA, cerebral venous thrombosis [CVT] and unspecified)	The estimated numbers and (rates of stroke/1,000 pregnancies) for 1994/95 and 2006/07, respectively were: Antenatal: 1,165 (0.15); 1,936 (0.22) At delivery: 2,042 (0.27); 2,401 (0.27) Postpartum: 878 (0.12); 1,956 (0.22) During the **antenatal** period from 1994-95, the most frequent types of stroke (number and rate/1,000 pregnancies) were hemorrhagic (n=305, 0.04), CVT (n=283,0.04) and ischemic (n=261,0.03) During the **antenatal** period from 2006-2007, the most frequent types of stroke (number and rate/1,000 pregnancies) were CVT (n=593, 0.07), ischemic (n=414, 0.05) and hemorrhagic (n=303, 0.01) During **delivery** from 1994-95, the most frequent types of stroke (number and rate/1,000 pregnancies) were CVT (n=955, 0.13), unspecified (n=283, 0.08) and ischemic (n=261, 0.03) During the **delivery** period from 2006-2007, the most frequent types of stroke (number and rate/1,000 pregnancies) were CVT (n=1,034, 0.12), unspecified (n=741, 0.09) and hemorrhagic (n=259,0.03) During **postpartum** period from 1994-95, the most frequent types of stroke (number and rate/1,000 pregnancies) were unspecified (n=286, 0.04), CVT (n=254, 0.03) and hemorrhagic (n=175, 0.02)

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				During the **postpartum** period from 2006-2007, the most frequent types of stroke (number and rate/1,000 pregnancies) were hemorrhagic (n=697, 0.08), CVT (n=469, 0.05) and SAH (n=389, 0.04)
Liang et al. 2006 **Taiwan** **Retrospective study**	During a 13-year period (1992-2004) there were 66,781 deliveries at a single institution.	Medical records were reviewed to identify the number of women who had suffered a stroke (ischemic or hemorrhagic) during their pregnancy, and up to 6 weeks postpartum.	Incidence and causes of stroke	There were 32 strokes (11 ischemic and 21 Intracranial hemorrhage). Incidence rates for total, ischemic stroke and ICH/100,000 were 47.9, 16.5 and 31.4, respectively. **Infarction:** Mean maternal age was 31.5 years. 9 patients were multiparous. None had a previous neurological history. Risk factors included cardiac disease (n=4), HTN (n=2), smoking (n=3) and hyperlipidemia (n=1). Most common etiologies were cardioembolism (n=4), central venous thrombosis (n=3), congenital heart disease (n=2) and pre-eclampsia/eclampsia (n=2). Symptom onset was pre-delivery (n=6, range 8-39 weeks) and postpartum (n=4, mean 8.5 days). **Intracranial hemorrhage**: Mean maternal age was 29.4 years. 14 patients were multiparous. None had a previous neurological history. Risk factors included cardiac disease (n=4), HTN (n=3), smoking (n=3) and hyperlipidemia (n=3). Most common etiologies were vascular anomalies (n=6), arteriovenous malformations (n=4), coagulopathy (n=4) and pre-eclampsia/eclampsia (n=5). Symptom onset was pre-delivery (n=17, range 14-38 weeks) and postpartum (n=4, mean 3.3 days).
Jaigobin & Silver 2000 **Canada** **Retrospective study**	During a 17-year period (1980-1997) there were 50,711 deliveries at a single institution.	Medical records were reviewed to identify the number of women who had suffered a stroke (ischemic or hemorrhagic) during their pregnancy, and up to 6 weeks postpartum.	Stroke incidence, stroke etiology and vascular risk factors	There were 34 strokes (21 ischemic and 13 Intracranial hemorrhage-7 SAH and 6 ICH). Event rates for total, ischemic stroke and ICH/100,000, adjusted for referrals outside of catchment area were 26, 18 and 8, respectively.

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Infarction: 15 patients were multiparous. There were 13 cases of arterial infarction and 8, of venous thrombosis. For all patients with infarction, the etiology was unknown in 11 cases. In the remaining cases, etiologies were coagulopathy (n=5), cardioembolism (n=4), and large artery (n=1). Vascular risk factors included pre-eclampsia/eclampsia (n=6), smoking (n=4) and HTN (n=1). 9/13 arterial events occurred in the 3rd trimester or puerperium, while 7/8 venous occlusions occurred postpartum. All patients survived. **Intracranial hemorrhage**: 5 patients were multiparous. There were 7 cases of SAH and 6 of ICH. The etiology was unknown in 2 cases. In the remaining cases, etiologies were aneurysm (n=3), AVM (n=5), and disseminated intravascular coagulation (n=2). Vascular risk factors included pre-eclampsia/eclampsia (n=1), and smoking (n=1). Timing of events was 1st trimester (n=2), 2nd trimester (n=6), 3rd trimester (n=2), and postpartum (n=4). 3 patients died.
Kittner et al. 1996 **USA** **Retrospective study**	During a 13-year period (1988-1991) there were 141,243 deliveries to women, aged 15-44 years, at 46 hospitals.	Medical records of women who were discharged from hospital with a diagnosis of ischemic or hemorrhagic stroke were reviewed and their pregnancy status at the time of stroke (and up to 6 weeks prior to its occurrence) was determined.	Stroke incidence, pregnancy-related stroke risk, stroke etiology and vascular risk factors	There were 28 strokes related to pregnancy during the study period, 17 infarcts and 14 ICH. Of these events, 3 infarcts and 1 ICH were related to abortions or stillborn births During the same period there were 175 infracts and 48 ICH in women, not related to pregnancy. **Infarctions:** Mean age was 27 years. There were no strokes that occurred during the 1st trimester, 1 during the 2nd, 5 during the 3rd trimester and 10 that occurred with 6 weeks postpartum. Etiologies were preeclampsia/eclampsia (n=4), vasculopathy (n=2), carotid dissection (n=10), thrombotic thrombocytopenic purpura (n=1), cortical vein thrombosis (n=1), postherpetic vasculitis (n=1) and unknown (n=6).

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Intracerebral hemorrhage (ICH): Mean age was 28 years. There were no strokes that occurred during the 1st trimester, 3 during the 2nd, 5 during the 3rd trimester, 1 within 24 hours of delivery and 8 that occurred with 6 weeks postpartum. Etiologies were AVM (n=3), preeclampsia/eclampsia (n=2), cocaine use (n=2), vasculopathy (n=1), vasculitis (n=1) and unknown (n=4). The risk of stroke, adjusted for age and race during pregnancy or within 6 weeks, compared with women who were not pregnant: Ischemic: RR=1.6, 95%CI 1.0-2.7 ICH: RR=5.6, 95% CI 3.0-10.5 Any stroke: RR=2.4, 95% CI 1.6-3.6 The risk of stroke, adjusted for age and race during 6 weeks after pregnancy, compared with women who were not pregnant: Ischemic: RR=5.4, 95% CI 2.9-10.0 ICH: RR=18.2, 95% CI 8.7-38.1 Any stroke: RR=7.9, 95% CI 5.0-12.7
Simolke et al. 1991 **USA** **Retrospective study**	89,913 women who delivered at a single hospital from 1984-1990.	Data were obtained through chart review	Stroke incidence	There were 15 strokes-6 cases of hemorrhagic stroke (4 ICH, 2 SAH) and 9 cases of ischemic stroke. Total estimated stroke rate per 100,000 deliveries was 16.6. Mean ages of women were 22 years (Ischemic stroke) and 25.3 years (hemorrhagic stroke). There were 3 maternal deaths (1 hemorrhagic, 2 ischemic). Timing of ischemic stroke was antepartum (n=5, 1st trimester, 2nd trimester 2, 3rd trimester 2) and postpartum (n=4, 1 day-2 weeks) Timing of hemorrhagic stroke was antepartum (n=5, all 3rd trimester) and postpartum (n=1, day 4)

Intracerebral Hemorrhage (ICH)

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Leffert et al. 2015 **USA** **Retrospective study**	330 pregnant women, aged 18-44 years, included in the Get With The Guidelines Stroke Registry, discharged from hospitals with a confirmed diagnosis of ICH or SAH from 2008-2014. 10,562 nonpregnant women admitted to hospitals during the same period, with a diagnosis of ICH or SAH.	The characteristics of pregnant vs. nonpregnant women who suffered an SAH or ICH were compared	Demographics, medical history, initial examination findings, medications use prior to admission and hospital outcomes	There were 178 cases of ICH among pregnant women vs. 4,817 among nonpregnant women. Pregnant women were significantly younger (median age 31 vs. 38, p<0.0001), were less likely to have suffered a previous stroke (2.8% vs. 12.6%, p<0.0001), or have coronary artery disease or a previous MI (0% vs. 2.7%, p=0.01). Pregnant women were also less likely to have diabetes (1.7% vs. 11.7%, p<0.0001), have hypertension (15.2% vs. 41.7%, p<0.0001) or dyslipidemia (1.7% vs. 6.8%, p=0.003). Pregnant women were significantly less likely to have taken antiplatelets, anticoagulants, antihypertensive agents or statins prior to admission Pregnant women had significantly lower in-hospital mortality (10.1% vs. 19.6%, p=0.002), and were more likely to be discharged home (56.2% vs. 47.2%, p=0.02) and be independent in ambulation on discharge (52.4% vs. 43.2%, p=0.02). In adjusted analysis, the odds of in-hospital mortality were significantly lower for pregnant women with ICH (OR=0.57, 95% CI 0.34-0.94)
Takahashi et al. 2014 **Japan** **Retrospective study**	97 women with occurrence of pregnancy-associated hemorrhagic stroke across 109 neurosurgical institutes in Japan from 2010-2011. Mean age was 32.2 $\pm$ 5	Chart review of all strokes occurring during pregnancy, delivery and puerperium (no later than weeks). Clinical information of interested included: stroke type and time of stroke onset (gestational age or time after delivery), causes of hemorrhage, types of underlying cerebrovascular	Patient prognosis was assessed using the modified Ranking Scale (mRS) at discharge.	60 (61.9%) ICHs occurred during pregnancy (mean gestational age at onset of hemorrhage: 27.7 $\pm$ 10.1 weeks), 13 (13.4%) occurred at delivery (mean deliver weeks: 38.4 $\pm$ 3.7 weeks) and 24 (24.7%) occurred during puerperium (time after delivery: <24 hours in 8 women; 1/3 days in 4 women; 3-7 days in 3 women; 8-42 days in 8 women; and unknown in 1). Detection rate of baseline CVDs before the 32nd week of gestation was significantly higher than

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
		diseases (CVDs), types of obstetric systemic complications, therapeutic procedures for stroke, methods of delivery, and maternal and neonatal prognoses.		after the 32nd week (90.0% versus 53.3%, p=0.0017) Causes of hemorrhage throughout all periods: Baseline CVDs: 5.75%, AVM: 25.8%, Aneurysms: 16.5%, Moyamoya disease (MMD): 10.3%, Other: 3.1% Obstetric complications: 12.4% Undetermined: 32.0% Causes of hemorrhage during pregnancy Baseline CVDs: 71.7%, 23 AVM ruptures, 13 aneurysmal ruptures AVMSs occurred 1.8 times the frequency of ruptured aneurysms Causes of hemorrhage at delivery Baseline CVDs: 23.1%, 2 AVM ruptures Causes of hemorrhage during puerperium Baseline CVDs: 33.5% Poor outcome – including 10 deaths – were seen in 36.1% of cases despite aggressive treatment. Pregnancy-associated hemorrhagic strokes frequently concealed baseline CVDs, especially when occurred before 21 weeks of gestation; AVMs were the predominant bleeding source. Close examination for cerebral vascular lesions is essential when a pregnancy-associated hemorrhagic stroke is detected.
Yoshimatsu et al. **2014** **Japan** **Cross-sectional study**	38 women with intracerebral hemorrhage occurring in pregnancy or postnatally. Mean age was 31.5 years	Nationwide survey of 1,582 facilities, which reported on the outcomes of women admitted with intracerebral hemorrhage in pregnancy or postnatally between January 1, 2006 and December 31, 2006. Response rate of 70% (N=1012 facilities) was achieved. Risk factors for ICH, neurological features,	Risk factors to ICH, onset to diagnosis time	Rate of ICH was 3.5 per 100,000 deliveries. There were 7 cases of maternal death (18.4% case mortality rate) Risk factors associated with ICH included re-eclampsia (n=10; 26.3%), hemolysis elevated liver enzymes and low platelet count (HELLP) (n=5), Moyamoya disease (n=4; 10.5%) and arteriovenous malformation (n=7; 18.4%)

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
		onset to diagnosis time (O-D time) and obstetric data were recorded.		Factors associated with poor outcome (modified Rankin Scale ≥3) included HELLP syndrome, moderately or severely disturbed consciousness at disease onset Factors associated with maternal mortality included: Pre-eclampsia, HELLP syndrome and O-D time >3 hours 32 patients underwent neurosurgery. The authors observed that maternal-fetal care centers do not always have full-time neurosurgeons or diagnostic imaging tools suitable for diagnosis of ICH. Their recommendation was that pregnant women with neurological symptoms should be transferred to a regional facility that are equipped to treat patients with ICH.
Bateman et al. 2006 **USA** **Cross-sectional study**	423 women aged 15 to 44 years with a diagnosis of ICH and who had also been coded for an antepartum, childbirth or fetal demise or postpartum condition (1993-2002) were identified from Nationwide Inpatient Sample.	Using US Census data, estimates were made of the rates of ICH in pregnant/postpartum and non-pregnant women. Rates and independent predictors of various risk factors and comorbidities in patients with pregnancy-related ICH were compared to the rates found in the general population of delivering	Frequency, risk factors and outcomes of intracerebral hemorrhage	The estimated rates of pregnancy-related ICH were: 6.1 pregnancy-related ICH per 100,000 deliveries 7.1 pregnancy-related ICH per 100,000 at-risk person-years (compared to 5.0 per 100,000 person-years for non-pregnant women in the age range considered) The increased risk of ICH associated with pregnancy was largely attributable to ICH occurring in the postpartum period. In-hospital mortality for pregnancy-related ICH was 20.3%. ICH accounted for 7.1% of all pregnancy-related mortality recorded in this database. Significant independent risk factors for pregnancy-related ICH included: Advanced maternal age (OR=2.11, 95% CI 1.69 to 2.64 African American race (OR=1.83, 95% CI 1.39 to

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				2.41) Preexisting hypertension (OR=2.61, 95% CI 1.34 to 5.07 Gestational hypertension (OR=2.41, 95% CI 1.62 to 3.59) Preeclampsia/eclampsia (OR=10.39, 95% CI 8.32 to 12.98) Preexisting hypertension with superimposed preeclampsia/ eclampsia (OR=9.23, 95% CI 5.26 to 16.19) Coagulopathy (OR=20.66, 95% CI 13.67 to 31.23) Tobacco abuse (OR=1.95, 95% CI 1.11 to 3.42).

Subarachnoid Hemorrhage (SAH)

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Leffert et al. 2015 **USA** **Retrospective study**	330 pregnant women, aged 18-44 years, included in the Get With The Guidelines Stroke Registry, discharged from hospitals with a confirmed diagnosis of ICH or SAH from 2008-2014. 10,562 nonpregnant women admitted to hospitals during the same period, with a diagnosis of ICH or SAH.	The characteristics of pregnant vs. nonpregnant women who suffered an SAH or ICH were compared	Demographics, medical history, initial examination findings, medications use prior to admission and hospital outcomes	There were 152 cases of SAH among pregnant women vs. 5,745 among nonpregnant women. Pregnant women were significantly younger (median age 32.5 vs. 39, p<0.0001). Upon initial evaluation, pregnant women were less likely to have an altered level of consciousness (17.8% vs. 26.6%, p=0.01), and were more likely to display no neurological symptoms (5.3% vs. 2.6%, p=0.04) and had significantly higher blood pressures. Pregnant women were also less likely to be a smoker (6.5% vs. 35.1%, p<0.0001), have hypertension (16.5% vs. 31.9%, p<0.0001) or dyslipidemia (0% vs. 4.5%, p=0.002). Pregnant women were significantly less likely to have taken antiplatelets, anticoagulants, or antihypertensive agents prior to admission

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Pregnant women had significantly lower in-hospital mortality (2.6% vs. 14.4%, p<0.0001), and were more likely to be discharged home (84.2% vs. 65.2%, p<0.0001) and be independent in ambulation on discharge (80.2% vs. 61.1%, p<0.0001). In adjusted analysis, the odds of in-hospital mortality were significantly lower for pregnant women (OR=0.17, 95% CI 0.06-0.45)
Bateman et al. 2012 **USA** **Cross-sectional study**	Women, aged 15 to 44 years, with a primary or secondary diagnosis of SAH, were identified using the Nationwide Inpatient Sample (1995-2008)	Potential risk factors from pregnancy-related SAH were identified by a survey of the published literature; the prevalence of these comorbid conditions and demographics were compared with pregnancy-related SAH and a control group of all delivery admissions that were not complicated by SAH. Outcomes and risk-factors were compared with age-matched, non-pregnancy women with SAH.	Incidence of antepartum and postpartum SAH, and independent risk factors	There were 639 cases of pregnancy-related SAH (538 per 1000,000 deliveries) SAH was associated with 4.1% of all pregnancy-related in-hospital deaths. More than ½ of the SAH cases occurred post-partum. Independent risk-factors for pregnancy-related SAH: Advancing age: 25-34 years vs. <25 years: OR=1.87, 95% CI 1.53-2.28, 35-44 years vs. <25 years: OR=3.29, 95% CI 2.62-4.12 African-American race vs. Caucasian: (OR= 3.28, 95% CI 2.65-4.07, Hispanic ethnicity vs. Caucasian: OR= 1.44, 95% CI 1.12-1.86 Hypertensive disorders: OR= 7.02, 95% CI 5.97-8.24 Coagulopathy: OR= 7.88, 9%5 CI 4.96-12.52 Tobacco abuse: OR= 2.39, 95% CI 1.71-3.33 Drug abuse: OR=1.76, 95% CI 1.09-2.85 Alcohol abuse: OR=2.68, 95% CI 1.04-6.93 Intracranial venous thrombosis: OR=179.39, 95% CI 110.81-290.92 Sickle cell disease: OR= 7.98, 95% CI 3.93-16.2

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Hypercoagulability: OR= 4.06, 95% CI 1.75-9.43 Compared with SAH in nonpregnant controls, pregnancy-related SAH had lower clipping/coiling rates (12.7% vs. 44.5%, p<0.001)
Roman et al. 2004 **France** **Case series**	Eight patients, 10 to 35 weeks' gestation, with previous normal pregnancy evolution, who presented between 1992 and 2000 to a single institution with SAH due to aneurysmal rupture.	-	-	Patients ranged in age from 27-40 years. Gestational age ranged from 12-38 weeks. Timing of treatment and maternal outcome: 1. Intravascular embolization immediately after caesarian section; favourable 2. Surgical clipping 1 day before cesarean section, favourable 3. Surgical clipping at 12weeks' gestation, favourable 4. Surgical clipping 3 days after cesarean section; favourable 5. Intensive care, no surgical intervention, death 6. Intravascular embolization 4 months after delivery, favourable 7. Intensive care, no surgical intervention, death 8. Surgical clipping 3 days after cesarean section, death 12 days post-op
Kizilkilic et al. 2003 **Turkey** **Case report**	Three cases of ruptured intracranial aneurysms during pregnancy, treated by minimal invasive endovascular approach	-	-	**Case 1:** 25-year-old woman was admitted with severe headache, neck stiffness and third nerve palsy during 10th week of pregnancy. Cerebral magnetic resonance imaging and angiographic examination (MRI and MRA) revealed diffuse SAH and posterior communicating artery (PCoA) aneurysm. Seven Gugliemi Detachable Coils (GDC)-18 coils were deployed using a balloon remodeling technique. Patient was discharged 5 days after the procedure and underwent an elective abortion 3 days later. After 1-month patient was patient free and 3rd nerve palsy had disappeared. **Case 2:** 39-year old woman developed severe,

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				progressively worsening headache during the 18th gestational week. Cerebral MRI revealed left frontobasal and intraventricular hemorrhage, and MRA revealed an aneurysm of the left internal carotid artery (ICA). Patient elected to undergo endovascular surgery after consultation. The aneurysm was completely occluded using a balloon-remodeling technique for insertion of six GDC-18 coils. Patient awoke with no apparent neurological deficits. Patient discharged on the 3rd day after the procedure. Patient's recovery was uneventful, and she delivered a healthy infant 4 months after procedure. **Case 3:** 26-year-old woman was admitted with severe headache during 28th week of pregnancy; pregnancy had followed ovulation induction. Cerebral MRI showed diffuse SAH. Endovascular treatment was performed; aneurysm was completed occulated with one GDG- coil. Patient awoke neurologically intact. Patient was discharged on the 5th day of endovascular procedure and delivered a healthy infant at 38 weeks.

Arteriovenous Malformation (AVM)

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
Porras et al. 2017 **USA** **Retrospective study**	270 women with AVMs, of whom 191 became pregnant before AVM obliteration. Mean age was 35 years. from one institution (1990-2015)	The annual hemorrhage rate was calculated by determining the ratio of hemorrhage counts to patient-years of follow-up during either the exposure (ie. during pregnancy or postpartum) or the nonexposure period (i.e., interval from birth until obliteration of AVM)	Annual hemorrhage rates during the pregnancy and nonpregnancy period.	There was a total of 191 pregnancies which occurred before AVM obliteration, of which 175 (91.6%) were term or pre-term deliveries and 16 (8.4%) were abortions. There were 149 hemorrhages (11,097 person-years follow-up). The annual frequency of hemorrhage was 1.34%. Of these, 9 occurred during pregnancy (n=8), one during 6-weeks post-partum and 140 during non-exposed periods.

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
				The risk of AVM rupture during pregnancy or the post-partum period was significantly higher compared with the non-pregnant period (5.7% vs. 1.3%, RR=4.43, 95% CI 1.98–8.65, p<0.001).
Liu et al. 2014 **China** **Case-crossover study**	979 female patients, aged 18-40 years with intracranial AMVs admitted to a single institution between 1960-2010, were included. Mean age was 26.1 years. From this sample, 393 patients with ruptured AVM were identified.	Medical charts reviewed. The total lifetime risk of AVM was estimated for women during the period of pregnancy or the puerperium (6 weeks) and during the time excluding pregnancy/puerperium.	Pregnancy- and puerperium-related AVM risks	Of the total sample of 979 women, 797 hemorrhages occurred during 25,578 patient-years of follow-up: Annual hemorrhage rate of 3.11%. There were 393 cases of AVM rupture, of which 12 occurred over 452 pregnancies; Hemorrhage rate of 2.65% per pregnancy or 3.32% per year. The odds ratio for rupture of AVM during pregnancy and puerperium was significantly lower compared with the control period (OR=0.71, 95% CI 0.61–0.82). Of the 12 pregnancy associated AVM ruptures, 6 occurred in the 2nd trimester, 5 in the 3rd and 1, postpartum. The mean gestational age was 26.3 weeks. 9 patients were treated with surgical interventions. There were no maternal deaths among these women. 3 patients were managed conservatively. There was 1 maternal death
Gross et al. 2012 **USA** **Retrospective study**	54 women admitted to a single institution from 2002-2010 with an angiographic diagnosis of an AVM.	Medical charts were reviewed. For women who were not pregnant, the annual hemorrhage rate was calculated as the ratio of the number of bleeds to total number of patient-years of follow-up. The annual rate hemorrhage during pregnancy was calculated as	Hemorrhagic stroke rates	Five hemorrhages in 4 patients occurred over 62 pregnancies. The hemorrhage rate was 8.1% per pregnancy or 10.8% per year. Over the remaining 2,461.3 patient-years of follow-up, only 28 hemorrhages occurred. The annual hemorrhage rate was 1.1%. The associated risk of hemorrhage during pregnancy was significantly increased (HR=7.91,

Study/Type	Sample Description	Method	Outcomes	Key Findings and Recommendations
		the ratio of total number of bleeds occurring during pregnancy and the number of patient years follow-up during pregnancy		95% CI 2.64-23.7, p<0.0001) when limiting the analysis to patient follow-up up to age 40

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