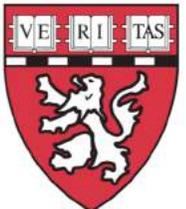


Neurosurgical Issues in Pregnancy

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Obstetrical Neurology Conference
September 7, 2018



Disclosures

None



Etiologies for Neurosurgical Emergencies

- Hemorrhage
 - Arteriovenous malformation
 - Aneurysm
 - Cavernous malformation
 - Moyamoya disease
 - Hypertensive disorders: HELLP/preeclampsia/eclampsia
- Tumor
- Trauma
- Hydrocephalus



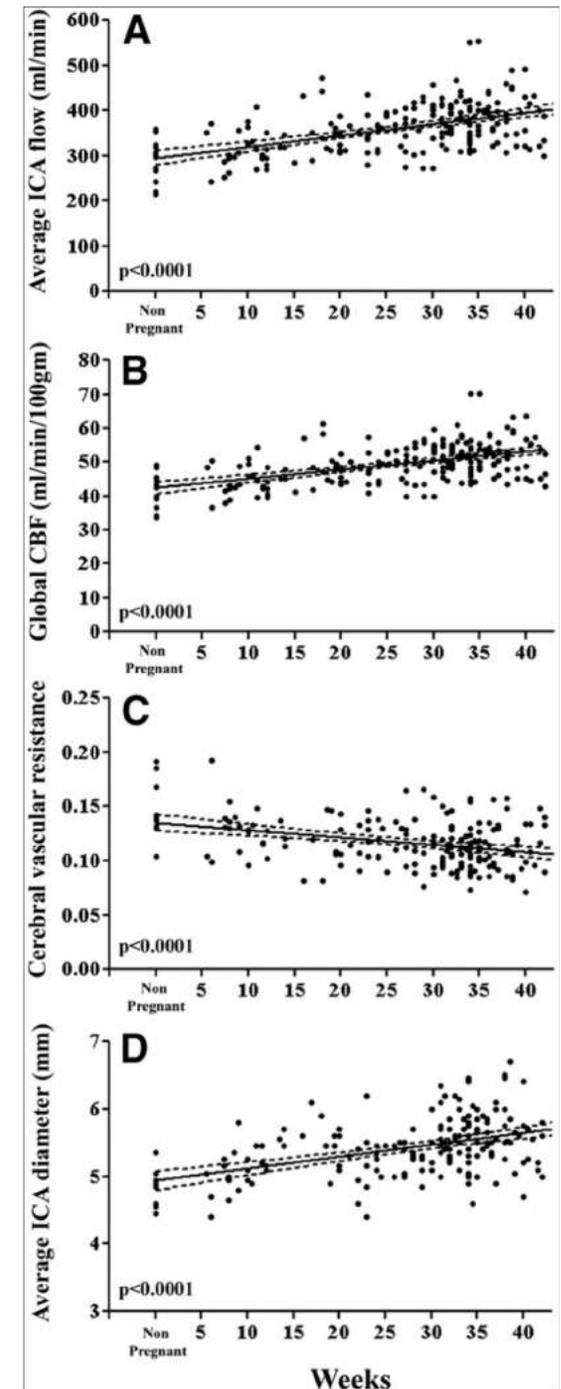
Types of Neurosurgical Lesions

Lesion		N = 33
Vascular	Aneurysm (SAH)	4
	AVM (ICH)	5
	dAVF (tinnitus)	1
	Cavernoma (hem)	1
Tumor	Glioma	9
	Meningioma	2
	Other	3
Trauma	MVA	4
Spontaneous ICH		2
Hydrocephalus		2



Maternal Cerebral Blood Flow

- Cardiac output increases at 3 months, peaks at 6 months and return to normal a few weeks after birth
- Circulating blood volume increases by 30-60% from first to second trimester
- Maternal CBF gradually increases during pregnancy



CT and MRI during Pregnancy

Modality	Recommendation
CT	ACOG and ACR: CT can be performed if deemed necessary after appropriate workup; adhere to ALARA principle.
Nuclear scintigraphy	ACOG: Use of $^{131}\text{I-NaI}$ is contraindicated during pregnancy. If diagnostic examination of the thyroid is essential, ^{123}I or $^{99\text{m}}\text{Tc}$ should be used instead of $^{131}\text{I-NaI}$. Cessation of breast-feeding is suggested after administration of gallium 67 (^{67}Ga) citrate and $^{131}\text{I-NaI}$. ICRP: Conception should be delayed until potential fetal dose from residual dose from radionuclides is less than 1 mGy.
US	ACR, ACOG, AIUM, SRU: US should be performed only when there is a valid medical reason; the lowest possible US output settings should be used.
MR imaging	ACOG: MR imaging is not associated with known adverse fetal effects. ACR: MR imaging can be performed in all trimesters if deemed clinically necessary and then only as an adjunct to initial US evaluation. MR imaging magnet strength should be $\leq 3\text{ T}$. ICNIRP, NRPB: It may be prudent to refrain from MR imaging during the first trimester of pregnancy.

ACOG = American Congress of Obstetricians and Gynecologists

ACR = American College of Radiology

AIUM = American Institute of US in Medicine

ICNIRP = International Commission on Non-Ionizing Radiation Protection

NRPB = National Radiological Protection Board in the United Kingdom

SRU = Society of Radiologists in Ultrasound.



Angiography during Pregnancy

Stage	Weeks gestation	Possible effects of radiation
Embryogenesis	0-2	Death (100 mGy)
Organogenesis	2-7	Congenital abnormalities (500 mGy)
Fetal	8-birth	Growth retardation, microcephaly, neuronal depletion, childhood cancer (120 mGy 8-15 wks, 250 mGy 16-25 wks, 500 mGy 26 wks to birth)

- Neuronal depletion is greatest during weeks 8 to 15
- No evidence of mutagenic or teratogenic effects of iodinated contrast (category B: no harm to animals, no human studies) (Puac et al, Magn Reson Imaging Clin N Am, 25:787-797, 2017)
- American College of Radiology does not recommend withholding iodinated contrast agents in pregnant women

Meyers et al., AJNR, 2000

Brent RL, Curr Probl Pediatr, 14:1-78, 1984

Kizilkilic O et al, Arch Gynecol Obstet, 268:325-328, 2003

Otake M et al., Int J Radiat Biol, 70:755-763, 1996

Stovall M et al, Med Phys, 22:63-82, 1995

Nagayama K et al, Asian J Neurosurg, 5:73-77, 2010

Lv X et al, Neuroradiol J, 28:385-388, 2015



Radiosurgery: Fetal Exposure

- Radiation dose from radiosurgery is below the safety threshold in pregnancy
- For a target dose of 20-25 Gy, lead shielding leads to fetal dose of 1.5-14 mGy

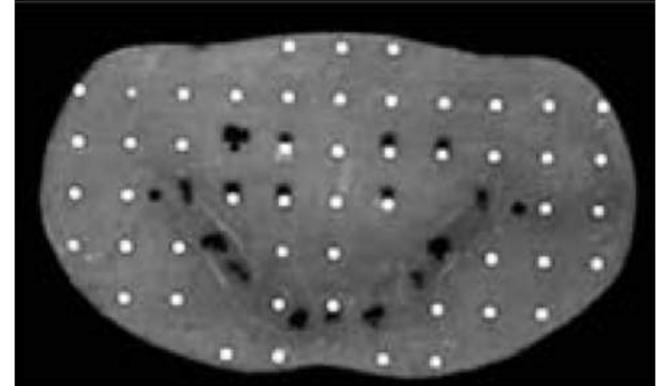


Figure 3. Cross section of an adult female RANDO phantom with 6 RPL-GRDs on the abdominal surface and 9 in the pelvic region to predict the location of the uterus and the fetus.

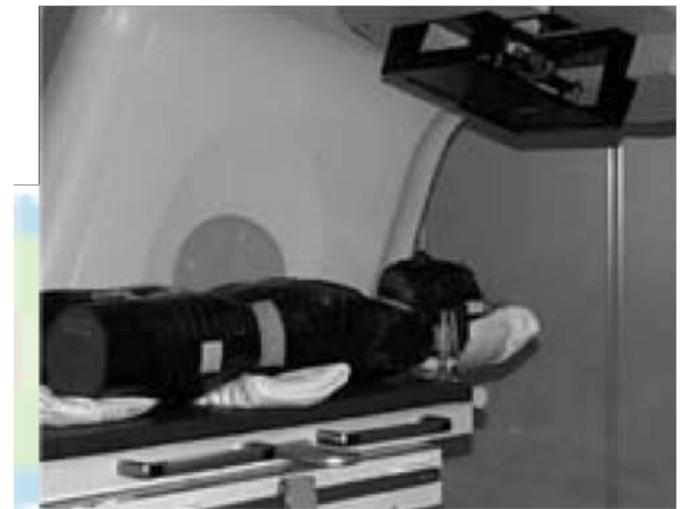


Figure 4. An adult female RANDO phantom on the LINAC table to measure the exposure doses to the inner pelvis after irradiation of the simulated cerebral AVM with 20Gy.

Nagayama et al, Asian J Neurosurg, 5:73-77, 2010

Lv X et al, Neuroradiol J, 24:383-388, 2015

Intracranial Hemorrhages during Pregnancy

- Intracranial hemorrhages during deliveries are rare: in ~60,000 deliveries: 21 ischemic strokes, 11 intracranial hemorrhages, of which 4 were due to AVMs (Skidmore et al, J Stroke Cerebrovasc Dis, 2001)
- 154 patients with ICH during pregnancy (Dias et al, Neurosurgery, 1990)
 - Aneurysms 77%
 - AVMs 23%



Intracranial Hemorrhages during Pregnancy

- 423 patients with pregnancy-related ICH from NIS 1998-2002
- 6.1 pregnancy-related ICH per 100,000 deliveries = 7.1 pregnancy-related ICH per 100,000 at-risk person-years
- 5.0 non-pregnancy related ICH per 100,000 person-years
- 58% of pregnancy-related ICH occurs in postpartum period

Risk Factor	OR
Coagulopathy	20.7
Preeclampsia/eclampsia	10.4
Preexisting hypertension	2.6
Gestational hypertension	2.4
Advanced maternal age (≥ 35)	2.1
Smoking	2.0
African American race	1.8

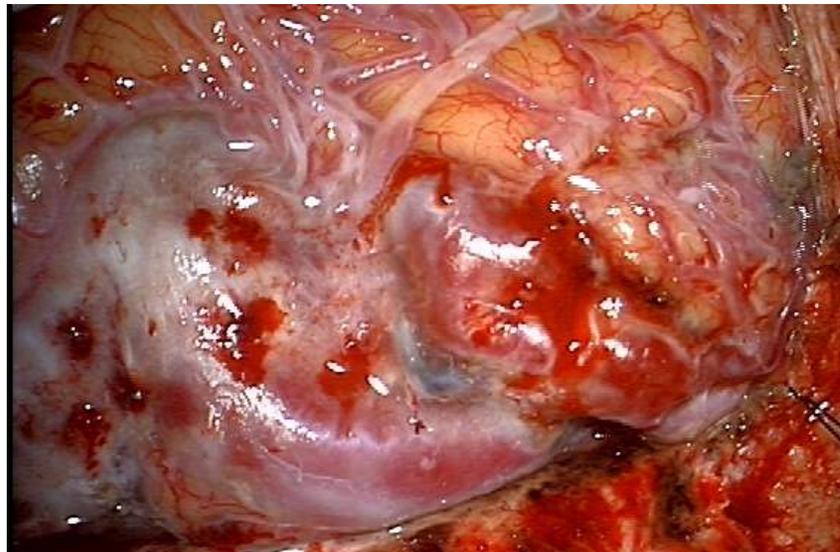
Outcome	%
Death	20
Routine	44
Home health care	6
Transfer to short term hospital	12
Other transfers	18



Arteriovenous Malformations

AVMs are a common cause of ICH in pregnancy

15-23% of peripartum intracranial hemorrhages from an intracranial lesion are due to AVMs (Dias et al, Neurosurgery, 1990; Cohen-Gadol et al., JNS, 2009)



Hemorrhage from AVMs during Pregnancy

There is increased risk of hemorrhage from AVMs during pregnancy

- Radiosurgical series report 3.5 – 9.3% hemorrhage rate during pregnancy compared with 3.1-4.5% when not pregnant (Horton et al, Neurosurgery, 1990; Forster et al, Stereotact Funct Neurosurg, 1993)

TABLE. Arteriovenous Malformation Hemorrhage Rates	
Cohort	%
Overall annual hemorrhage rate	1.5
Overall annual rebleed rate	7.3
Annual hemorrhage rate for females	1.3
Annual hemorrhage rate when not pregnant	1.1
Annual hemorrhage rate during pregnancy	10.8
Hemorrhage rate per pregnancy	8.1

Hemorrhage from AVMs during Pregnancy

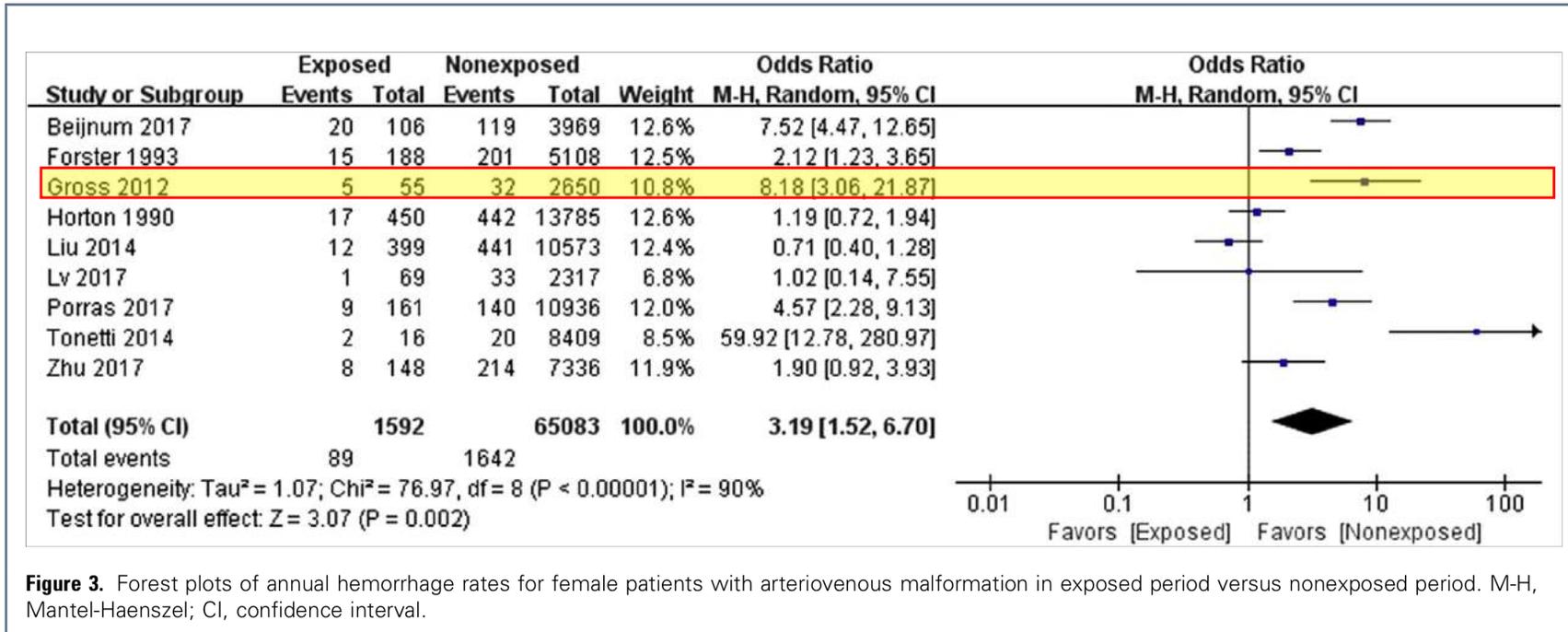


Figure 3. Forest plots of annual hemorrhage rates for female patients with arteriovenous malformation in exposed period versus nonexposed period. M-H, Mantel-Haenszel; CI, confidence interval.

Meta-analysis shows increased risk of hemorrhage (OR 3.2) during pregnancy



Management of Ruptured AVMs in Pregnancy

In 35 cases of peripartum intracranial hemorrhages from AVMs
(Dias et al, Neurosurgery, 27:855-865, 1990)

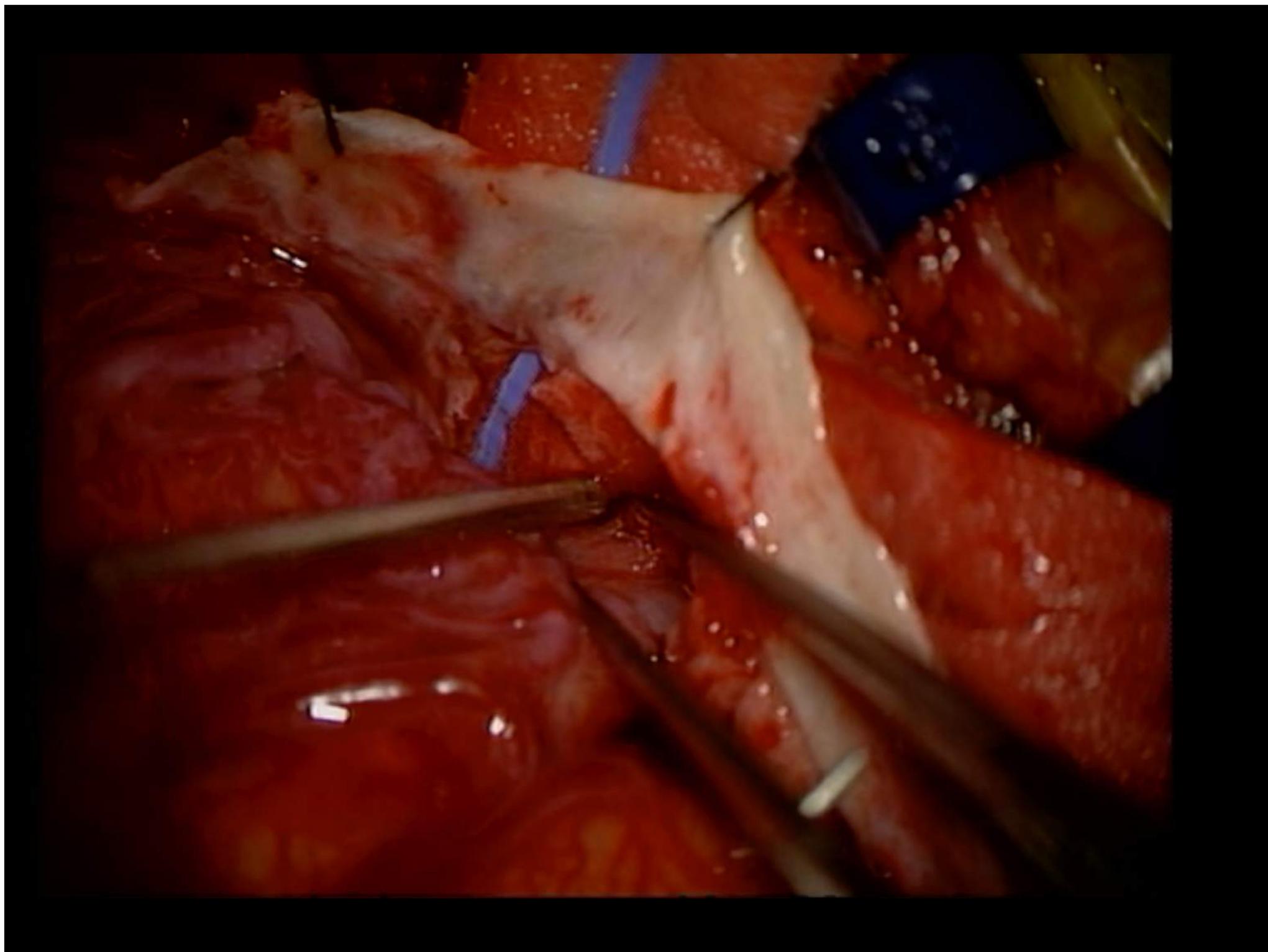
- Mean gestational age of 30.0 weeks
 - Conservative management: 32% maternal mortality, 23% fetal mortality.
 - Surgery: 23% maternal mortality, 0% fetal mortality
 - No statistically significant difference between C-section and vaginal delivery but likely underpowered
-
- AVMs tend to hemorrhage in the second and third trimester
 - Conservative management results in increased fetal and maternal mortality
 - Risk of vaginal delivery vs C-section unclear



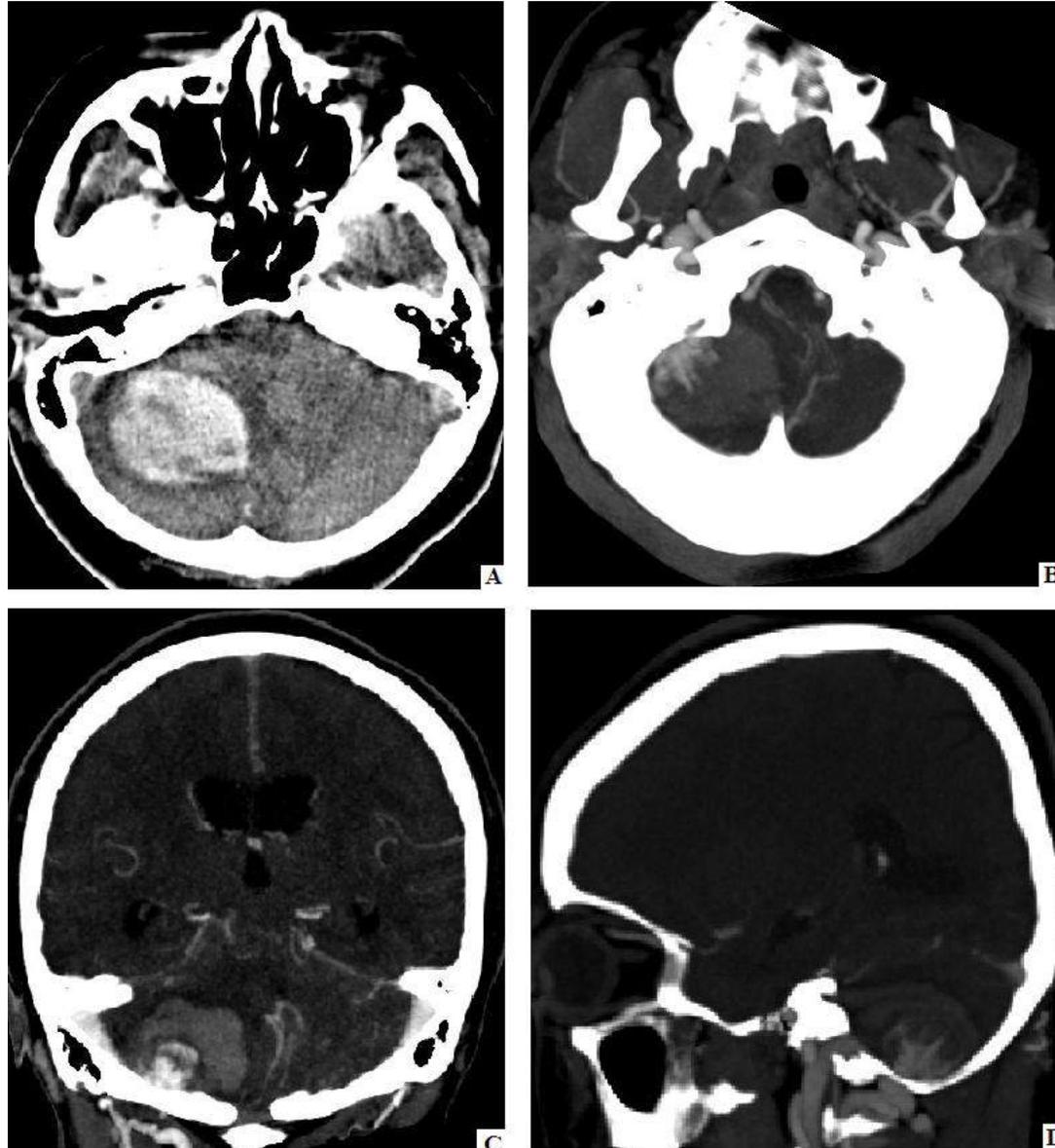
Management of Ruptured AVMs in Pregnancy

- **Neurosurgical emergency** (herniation, acute hydrocephalus)
 - Operate (decompression, resection, ventriculostomy/shunt)
- **Non-neurosurgical emergency**
 - Operable AVM
 - Consider risk to fetus vs rehemorrhage risk
 - Operate vs observe
 - Non-operable AVM
 - Observe





39-year-old G1P0 at 38 weeks gestation presents with acute headache, lethargy, and confusion

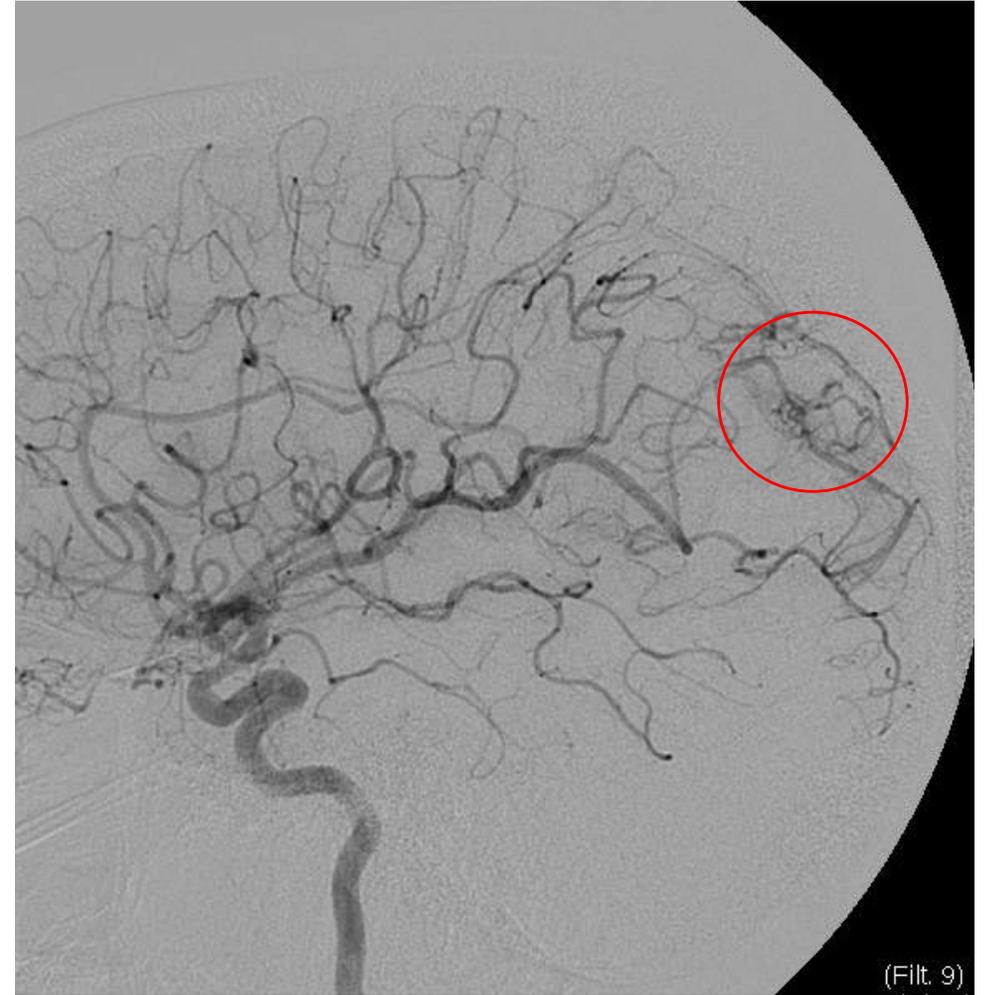
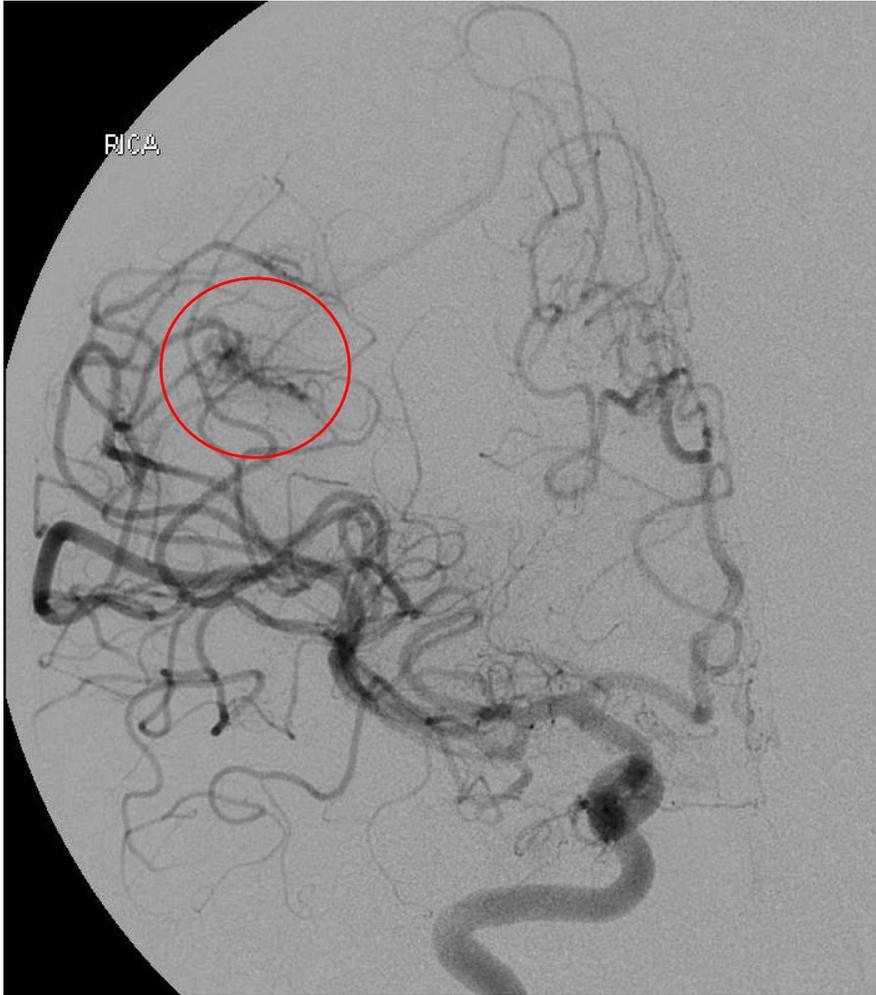


- Emergent Caesarean-section with concurrent external ventricular drain placement
- Followed by craniotomy for clot evacuation and resection of AVM
- At 1.5 yr followup, had mild left facial weakness and ataxic speech

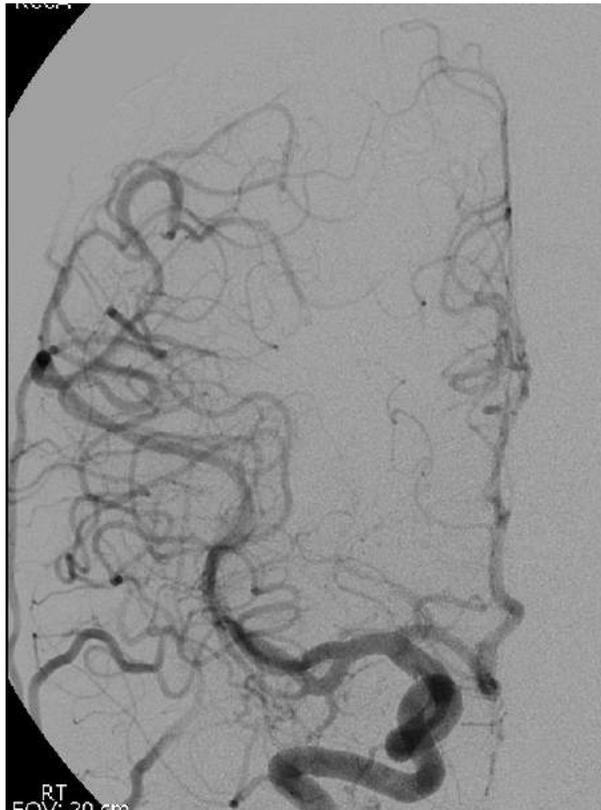


29-year-old G1P0 at 28 weeks gestation presented with acute headache and homonymous hemianopsia



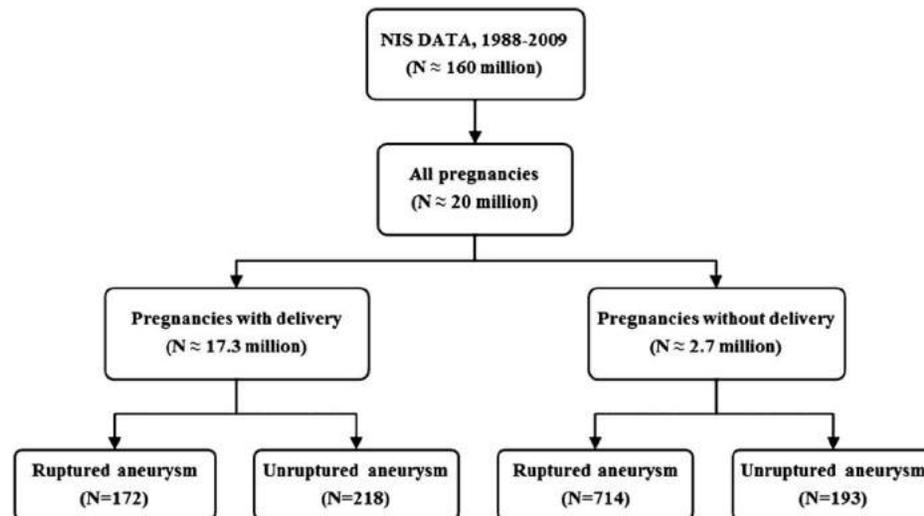


- Underwent surgical resection of AVM with eventual resolution of visual field defect
- Delivery at 36 weeks gestation.
- At 2 years followup, child is healthy and patient is neurologically intact.

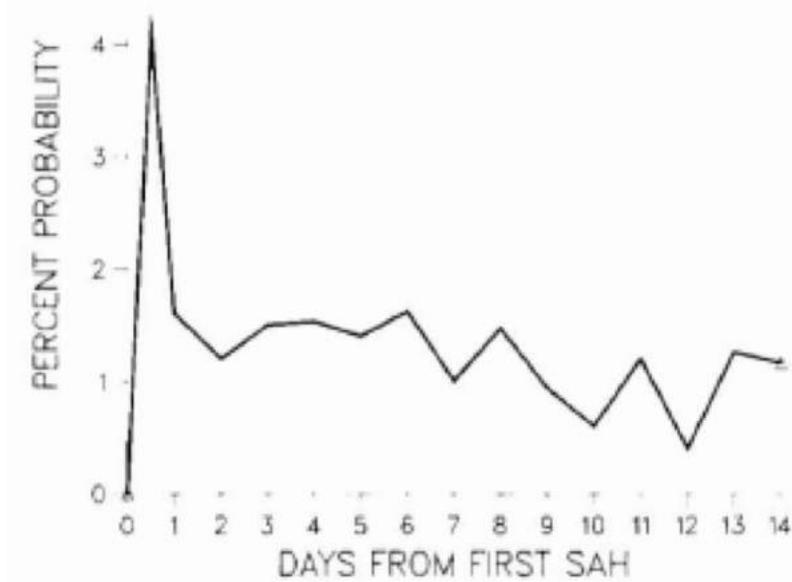


Aneurysms

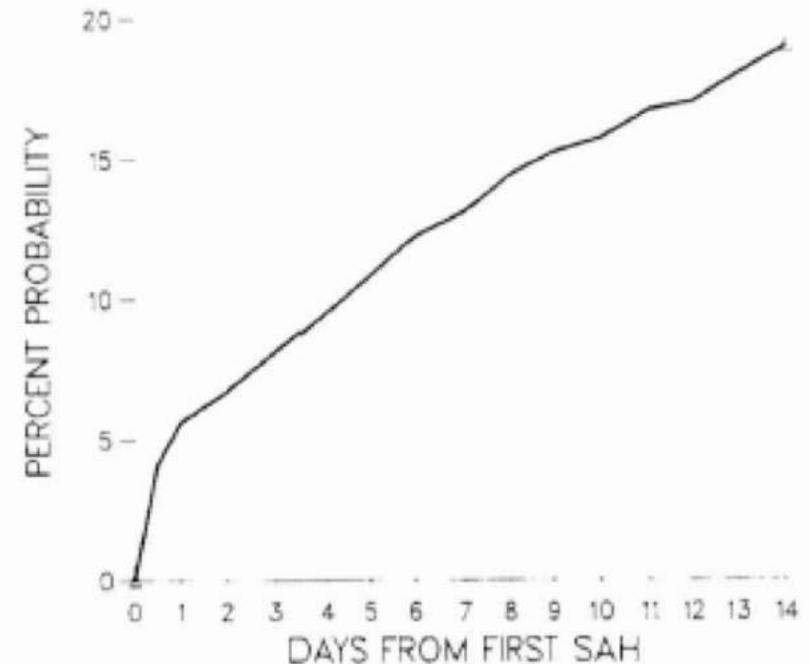
- Using NIS, risk of rupture during pregnancy = 1.4%, during delivery = 0.05% (Kim YW et al, Neurosurgery, 72:143-149, 2013)
- **The risk of rupture of intracranial aneurysms during pregnancy and delivery is not increased (RR 0.4, 95% CI 0.2-0.9)** (Tiel Groenestege et al, Stroke, 40:1148-1151)
- Rate of cesarean sections in patients with aneurysms is 70%



Risk of Aneurysm Rerupture



Daily risk of rerupture

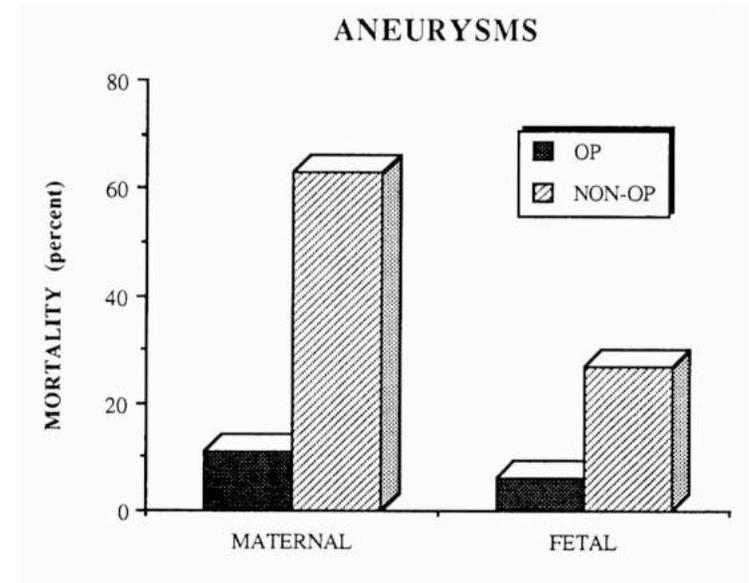


Cumulative risk of rerupture:
20% at 2 weeks

Aneurysms should be treated within 48 hours of presentation

Ruptured aneurysms in pregnancy

	Maternal mortality	Fetal mortality
No treatment of ruptured aneurysm	63%	27%
Treatment of aneurysm	11%	5%



Neurosurgical considerations should take precedence over obstetrical considerations in ruptured aneurysms

Management of Ruptured Aneurysm in Pregnancy

- Ruptured aneurysms should be treated within 48 hours
- Consider MRA for initial evaluation
- Minimize contrast load and radiation during angiography (eg. limit to single vessel angiogram)
- Weigh additional risks of endovascular coiling when considering surgical clipping vs endovascular coiling



Characteristics	
Age	31.5 (20-42)
Third trimester	73%
Second trimester	19%
First trimester	8%
Gestation	29.0 weeks
Presentation	
GCS	12.8
Hunt and Hess	2.7
Imaging	
CTA	9 (17%)
DSA	31 (60%)
MRA	3 (6%)

Characteristics	
Treatment modality	
Clipping	54%
Coiling	37%
None	10%
Delivery timing	
Before treatment	25%
At the same time as treatment	22%
After treatment	31%
At term	15%
Aborted	2%
Death in utero (maternal death)	4%
Delivery mode	
C-section	72%
Emergency	70%
Vaginal	26%

Pooled analysis from 23 studies, N=52

Ruptured aneurysms tend to present in 3rd trimester

Delivery occurred before or during treatment of aneurysm in 47%

Most patients underwent C-sections



Maternal and fetal outcome	
Glasgow outcome score	
4-5 (good)	85%
1-3 (severe disability or death)	16%
Apgar	
>=4 (good)	84%
0-3	16%
death	11%

GOS	
1	Death
2	Persistent vegetative state
3	Severe disability (need help with daily living)
4	Moderate disability (no need for help with daily living)
5	Low disability

	0	1	2
Appearance	Blue or pale everywhere	Acrocyanosis	No cyanosis
Pulse	Absent	< 100/min	>100/min
Grimace (to stimulation)	No response	Grimace	Cry
Activity	None	Some flexion	Flexion, resistance to extension
Respiration	Absent	Weak	Strong, cry

Maternal Outcome

	GOS 1-3 (N=8)	GOS 4-5 (N=44)	p
Treatment modality			0.329
Clip	2	25	
Coil	3	16	
None	3	3	
Delivery time			0.570
After tx	0	15	
At term	0	7	
Before tx	5	7	
Concurrent with tx	0	11	
No treatment	2	1	
Aborted or death in utero	0	1	
Delivery mode			0.263
Vaginal	1	11	
C-section	4	30	
None	2	1	
Hunt and Hess	3.9	2.5	0.052
Admission GCS	7	14	0.481
General complications	86%	23%	0.905
Maternal age	36	31	0.054
Trimester	3 rd (8)	1 st (14), 2 nd (10), 3 rd (30)	0.056

No association with mode of delivery or timing of delivery

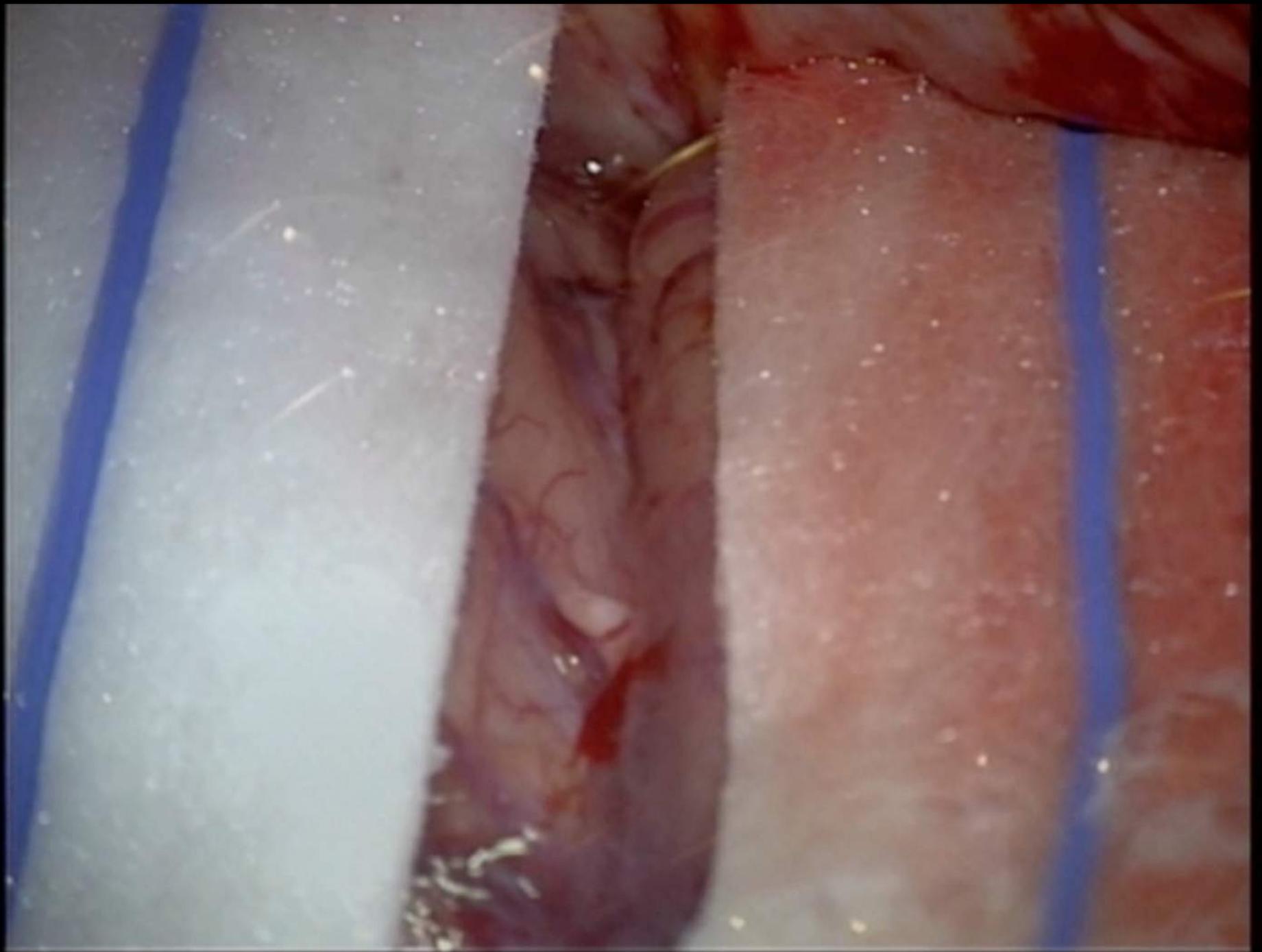
Robba et al., World Neurosurgery, 2016
 Kim et al., Neurosurgery, 2013
 Dias et al., Neurosurgery, 1990

Fetal Outcome

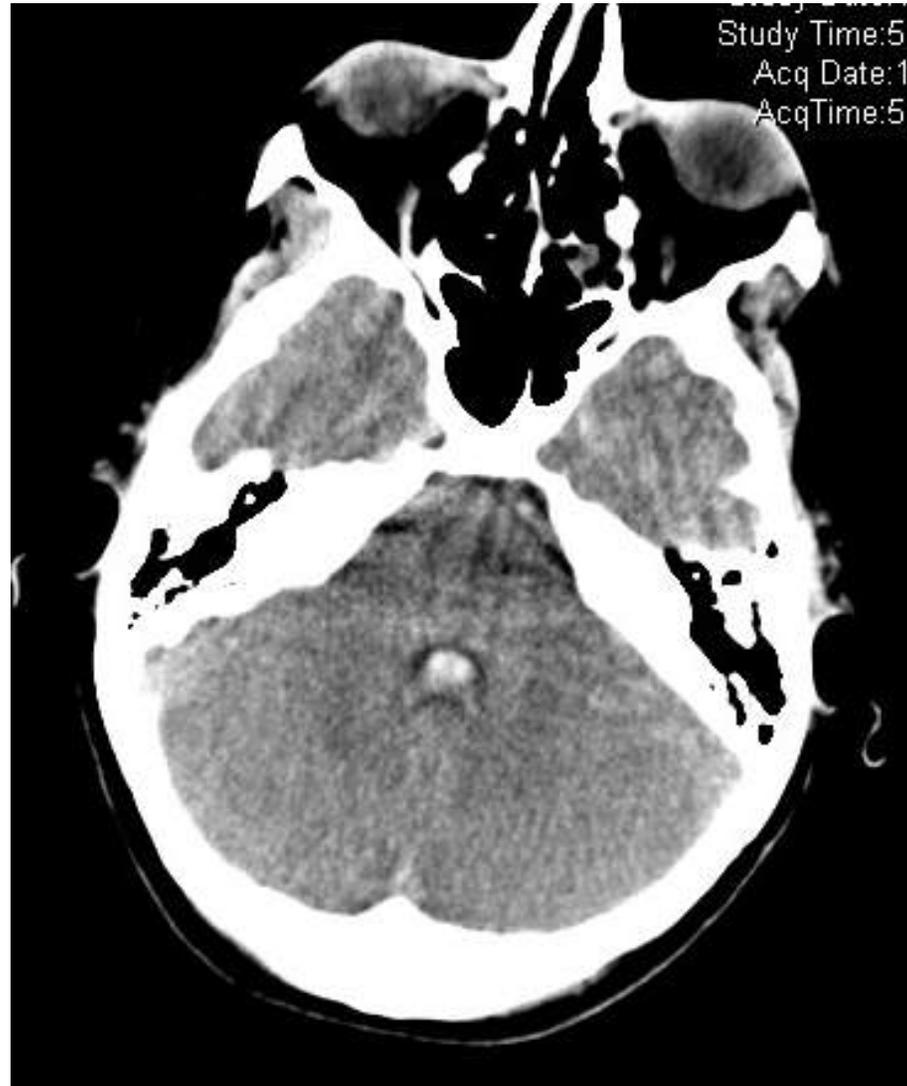
	Apgar 0-3 N=7	Apgar 4-10 N=37	p
Mode of delivery			0.125
Vaginal	1	9	
C-section	3	28	
None	3	0	
Timing of delivery			0.182
After treatment	1	14	
At term	0	7	
Before treatment	3	4	
Concurrent with treatment	0	12	
No treatment	3	0	
Aborted or death in utero	0	0	
Hunt and Hess grade	3.5	2.5	0.059
Treatment modality			0.116
Clip	1	22	
Coil	3	15	
None	3	0	

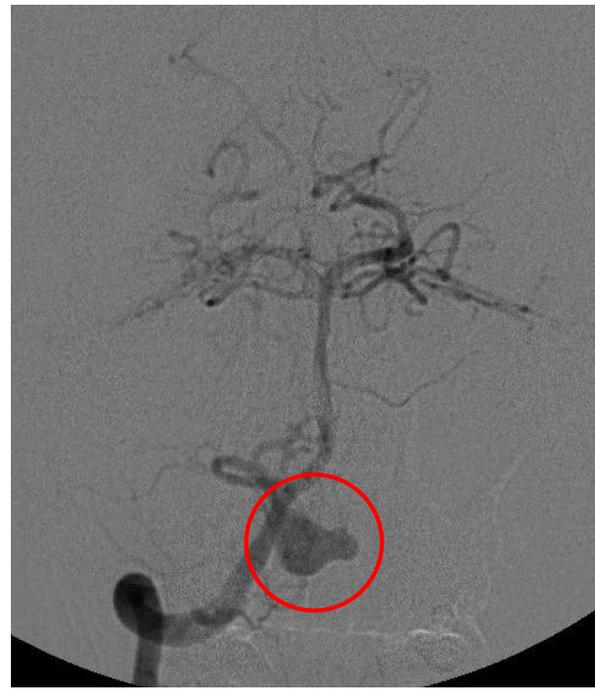
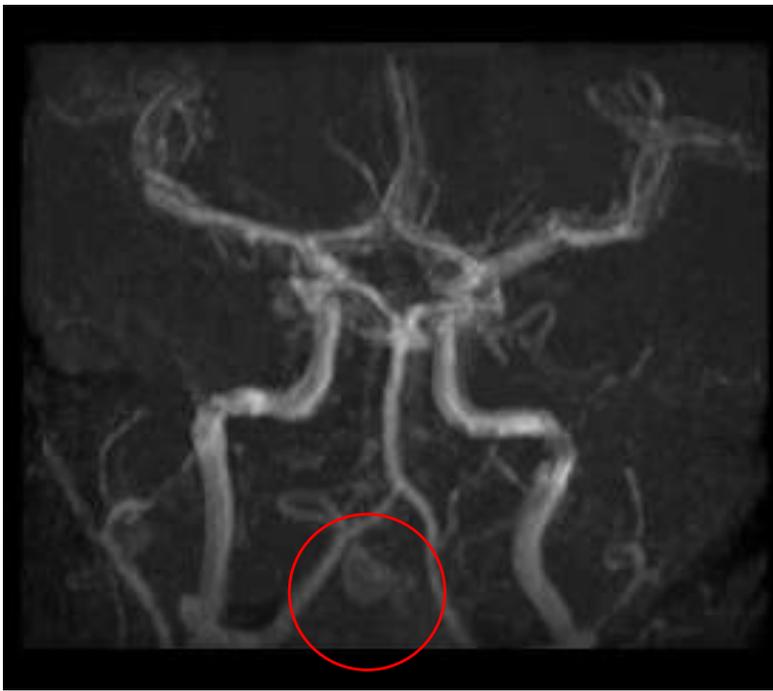
No association with mode of delivery or timing of delivery

Robba et al., World
Neurosurgery, 2016



34 yo woman, 18 weeks gestation, presents with acute headache then lethargy







The patient recovered well and was neurologically intact 3 weeks post-SAH. She delivered a healthy baby 5 months later.

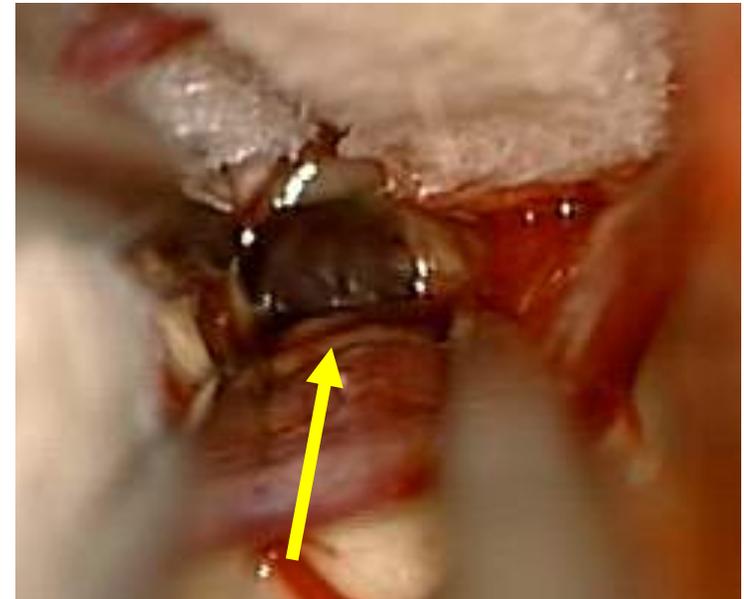
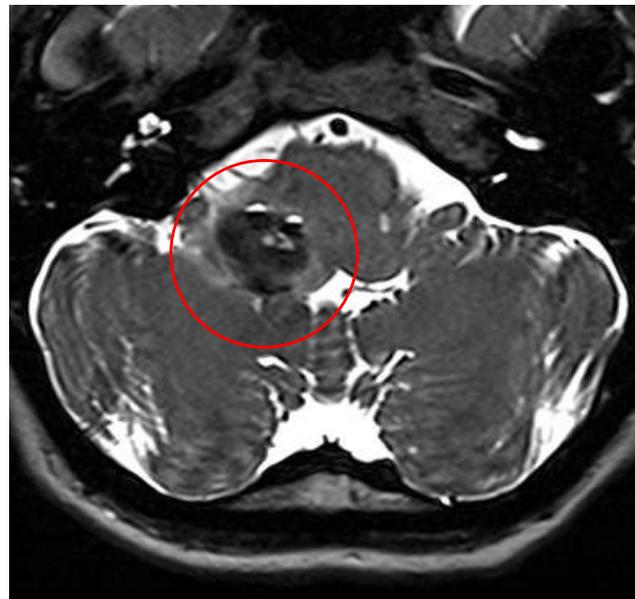
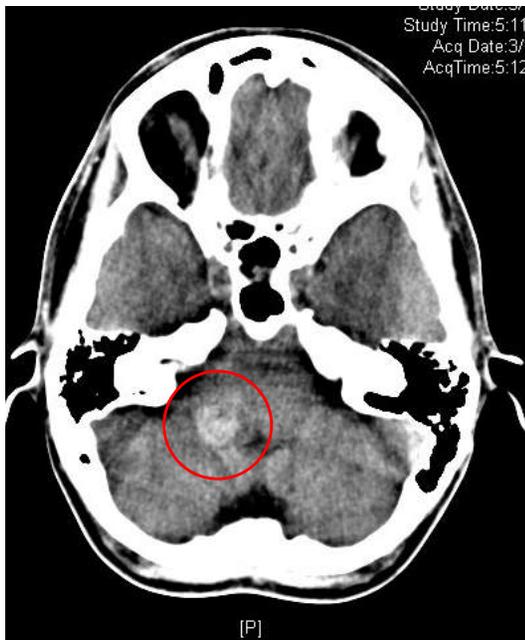
Cavernous Malformations

Natural History

- Incidence of cavernous malformations 0.4% (from 52,770 cases in MRI and autopsy studies)
- Risk of hemorrhage 2.4%/patient-year, 0.7%/lesion-year

Indications for surgery

- Symptomatic hemorrhage
- Seizures



Gross and Du et al., Neurosurg Focus, 30:E24, 2011

Gross and Du, JNS, 126:1079-1087, 2017

Cavernous Malformations

Risk in pregnancy

- 168 pregnancies in 64 women with cavernous malformations (Kalani and Zabramski, JNS, 2013)
- Risk of hemorrhage per pregnancy = 3% (1.8% in sporadic group, 3.6% in familial group)
- Vaginal deliveries performed without complications in 149 pregnancies

- 349 pregnancies (Witiw et al, Neurosurgery, 2012)
- Risk of hemorrhage per person-year 1.13% in pregnant women, and 1.01% when nonpregnant

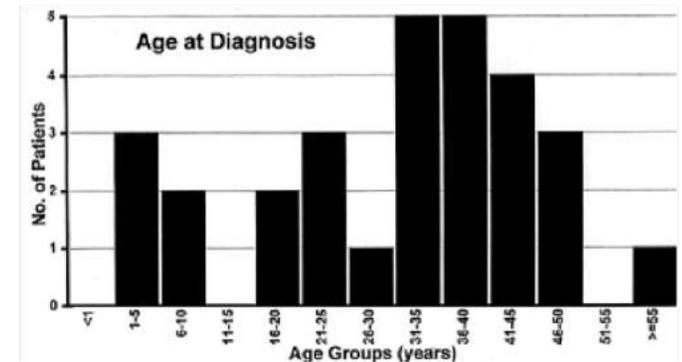
Management in pregnancy

- **Risk of symptomatic hemorrhage from cavernous malformations is not increased during pregnancy**
- **History of cavernous malformations is not a contraindication to pregnancy or vaginal delivery**
- **Emergent/urgent surgery rarely indicated**



Moyamoya

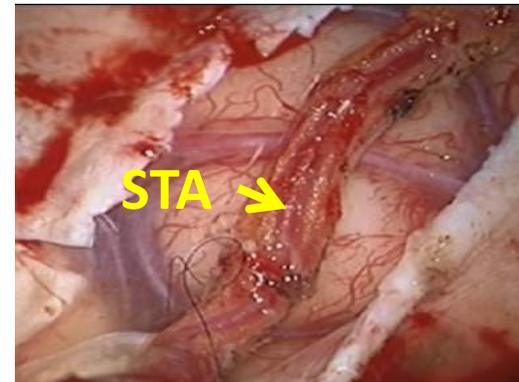
- Idiopathic progressive intracranial arterial stenosis (typically ICA, MCA)
- Predominance in East Asian population
- Incidence:
 - Japan: 0.94/100,000 (Baba et al, JNNP, 2008)
 - US: 0.09/100,000 (Uchino et al, Neurology, 2005)
- Bimodal peaks: 5 years and 20s-30s
- 2:1 female:male ratio
- Incidence rate ratios: Asian 4.6, black 2.2, white 1, Hispanic 0.5
- 10% familial (in Japan) and autosomal dominant with incomplete penetrance
- Annual stroke/hemorrhage risk in adults per patient:



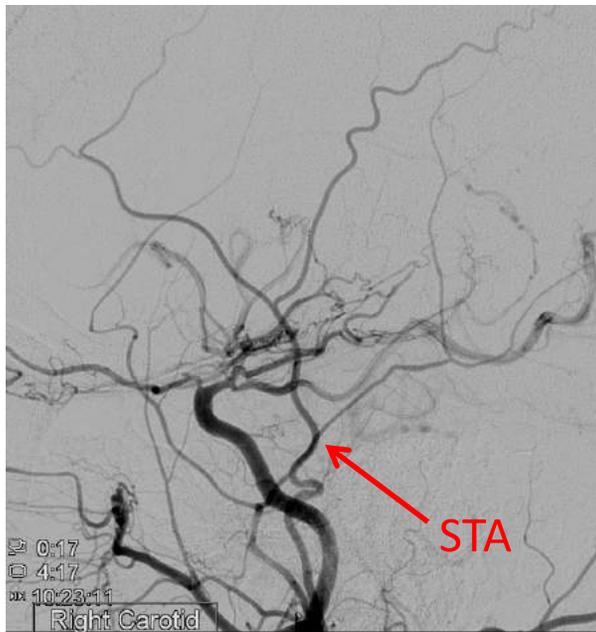
	No treatment	Bypass
Stroke	12%	5.4%
Hemorrhage	2.7%	0%

Moyamoya: Treatment

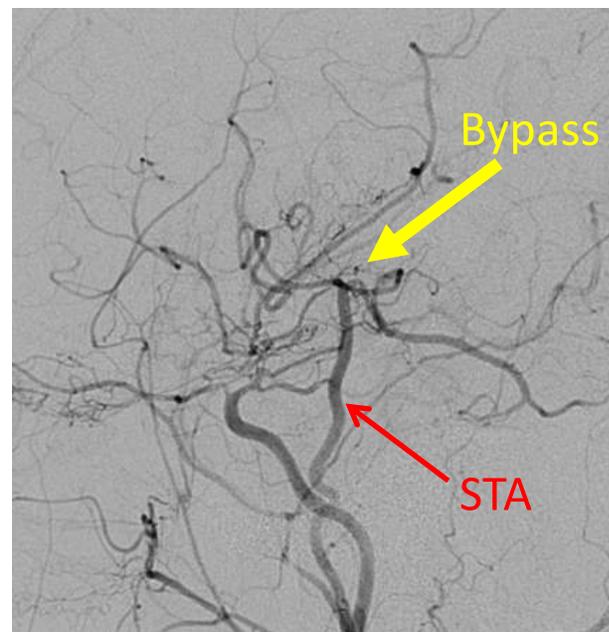
1. Indirect bypass: pial synangiosis



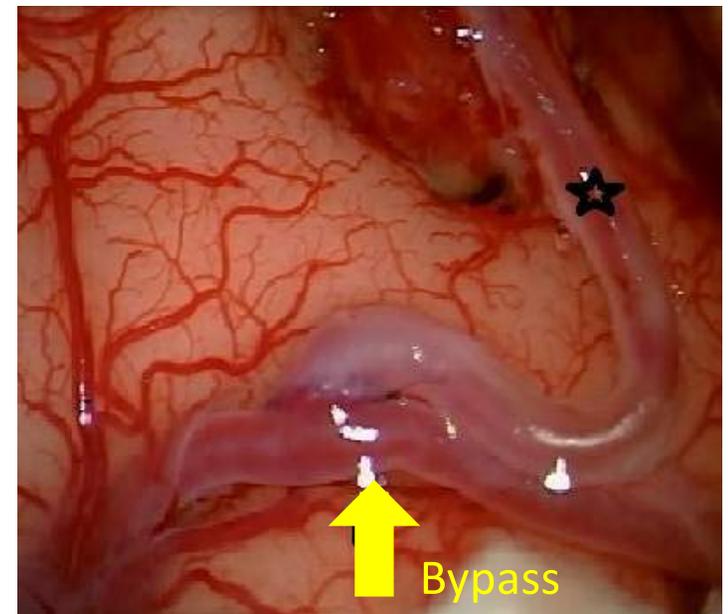
2. Direct bypass: superficial temporal artery to middle cerebral artery bypass



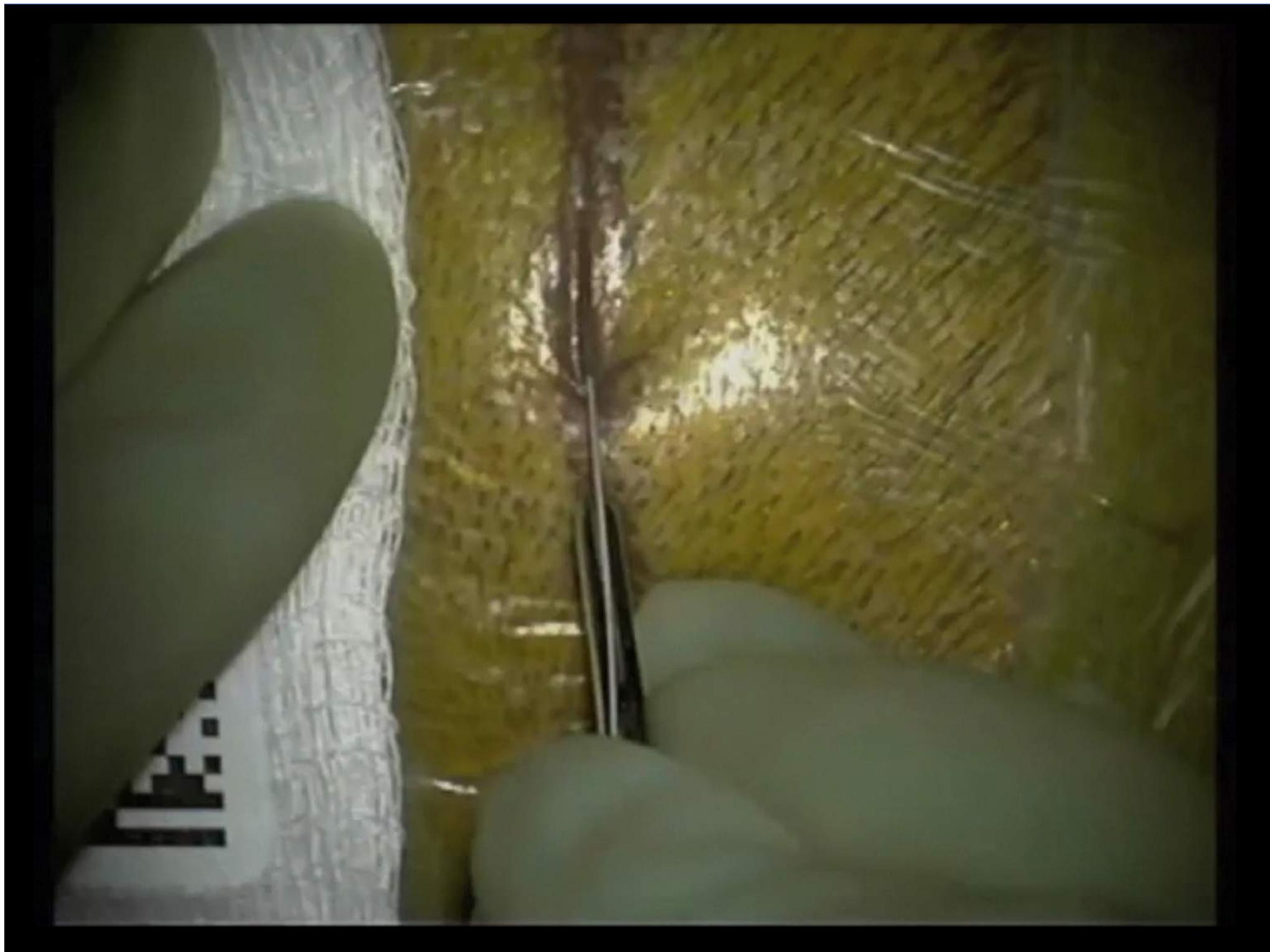
Preop



Postop

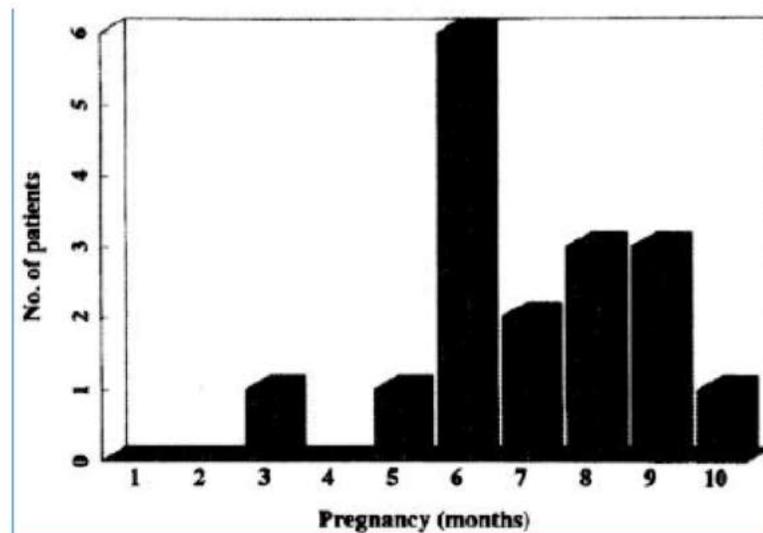


Intraop



Moyamoya

- 50 pregnancies in patients with **known** moyamoya disease, 1 had poor outcome (IVH at 30 weeks gestation, akinetic mutism, no bypass done), 6 with TIAs, 1 with seizures, 1 ICH
 - Maternal outcome: 44 good outcome, 1 akinetic mutism
 - Fetal outcome: all good outcome
- 25 patients with **undiagnosed** moyamoya, 16 with ICH, 5 with seizures/TIAs.
 - Maternal outcome: 3 deaths, 8 poor outcome, 12 good outcome.
 - Fetal outcome: 2 deaths, 15 good recovery, 1 hemiparesis
- **ICH mainly occurs in second or third trimester**
- **Much worse outcome when undiagnosed**



Fukushima et al, J Clin Neurosci, 2012
Komiya et al, Neurosurgery, 1998



	Diagnosis before pregnancy (N=96)	Diagnosis during pregnancy (N=23)
Age at MMD diagnosis	17 +/- 9	
Presentation		
Ischemic	83%	35%
Hemorrhagic	17%	65%
Treatment	Treatment before pregnancy	Treatment during pregnancy
bypass	69%	57%
none	31%	43%
Age at pregnancy	29 +/- 6	29 +/- 5
Neurological events	11%	43%
Mode of delivery		
Elective cesarean	58%	40%
Emergency cesarean	6%	40%
Vaginal	35%	20%
Delivery anesthesia		
Epidural/spinal	84%	27%
General	14%	73%
Unknown	2%	
Maternal neurological outcome		
Good	95.2%	73%
Mild	4.7%	5%
Severe	0%	9%
Death	0%	14%
Adverse fetal outcome		
NICU but recovered	0%	12%
Death	0%	24%

Management of Moyamoya in Pregnancy

- Cesarean section is the preferred method of delivery to avoid hypertension and hyperventilation but there is no evidence to support cesarean section over vaginal delivery
- Management during delivery: maintain normocapnia and normotension
- Neurological events may occur postpartum
- Bypass surgery is not indicated in the immediate post-ICH period
- Surgical intervention similar to nonpregnant patients (decompression, ventriculostomy)



Trauma

- Treat similarly to nonpregnant patient
- ICP management: decompressive craniectomy vs medical management
- Mannitol: pregnancy category B (no harm to animals, no human studies)
- Hypertonic saline: pregnancy category C (no studies in animals or humans)



Tumors

- Relative frequency of brain tumors in pregnancy is not increased and occurs rarely in pregnancy (Roelvink NCA et al., Arch Neurol, 1987)
- 8 women diagnosed with malignant brain tumors during pregnancy and 2 postpartum (1978-1998, 5 hospitals) out of 312,645 deliveries
- All 8 women with neurologic crisis with death in 4 and poor outcome in 2



Age	Wks gestation presentation	Presentation	Weeks gestation delivery	Symptoms at delivery	Tumor	Treatment	Baby outcome	Maternal outcome
22	28	N/V	40	herniation	Cerebellum, AA	Emergency CS	viable	death
19	26	N/V, L HP, coma	28	herniation, fetal distress	Parietal, AA	Emergency CS	died in NICU	death
27	30	AMS	34	MLS, HCP	Frontoparietal, GBM	Emergency CS Tumor resection	viable	alive with deficits
19	26	Brain death	27	respiratory arrest	temporal, midbrain, AA	Emergency CS	viable	death
24	27	HA	31	herniation	temporo-parieto-occipital, GBM	Emergency CS Tumor resection	viable	alive with deficits
37	28	N/V	34	herniation, respirator arrest	Cerebellum, breast CA	Emergency CS Decompression	viable	death
37	27	seizure	35		Frontotemporal, GBM	Elective CS Tumor resection	viable	alive
33	31	seizure	32		Frontal, GBM	Elective CS Tumor resection	viable	alive

Tewari et al., Am J Obstet Gynecol, 2000

Management of Tumors in Pregnancy

- Benign and asymptomatic:
 - Observe
- Malignant and/or symptomatic (esp from mass effect):
 - Treat



Hydrocephalus

Onset of hydrocephalus during pregnancy

- Acute hydrocephalus: external ventricular drain
- Shunt options:
 - Ventriculoperitoneal shunt
 - Ventriculopleural shunt
 - Ventriculoatrial shunt
- Endoscopic third ventriculostomy for obstructive hydrocephalus

Pre-existing shunts

138 pregnancies in 70 patients with existing shunts (Liakos et al, Neurol Res, 22:69-88, 2000):

- shunt malfunction and revisions occurred in 18 patients before delivery out of 138 shunt-dependent pregnancies
- May occur because of increased intra-abdominal pressures



Summary

Aneurysms:

- Incidence of ruptured aneurysms in pregnancy and delivery is rare (~1/50,000)
- Pregnancy and delivery do not increase the risk of aneurysm rupture
- Untreated ruptured aneurysms are associated with high maternal and fetal morbidity and mortality -> ruptured aneurysms in pregnancy should be treated according to neurosurgical considerations
- Mode and timing of delivery have no association with maternal or fetal outcome

AVMs:

- Increased risk of hemorrhage in the second and third trimester
- Conservative management of ruptured AVMs results in increased fetal and maternal mortality
- Risk of vaginal deliver vs C-section unclear

Cavernous malformations:

- Risk of symptomatic hemorrhage from CCM is not increased during pregnancy
- History of CCM is not a contraindication to pregnancy or vaginal delivery
- Emergent/urgent surgery rarely indicated

Moyamoya:

- Intracerebral hemorrhage mainly occurs in second or third trimester
- Much worse maternal and fetal outcome when undiagnosed



Thank You



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WOMEN'S HOSPITAL



HARVARD
MEDICAL SCHOOL

