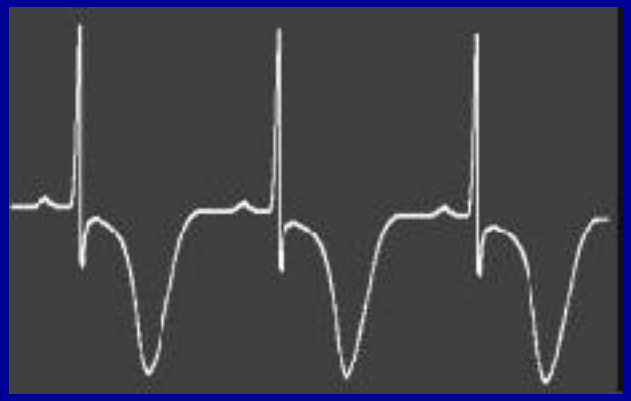
Left Ventricular Dysfunction After Subarachnoid Hemorrhage



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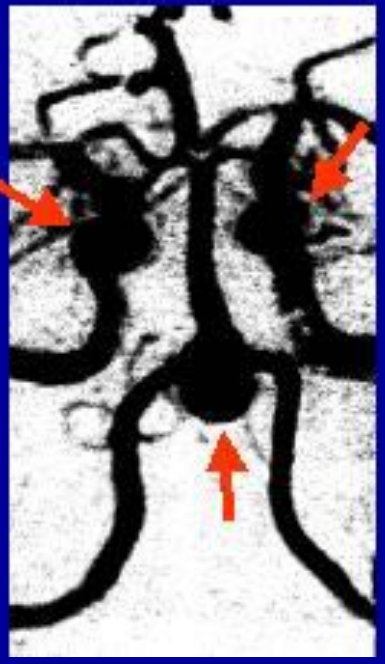
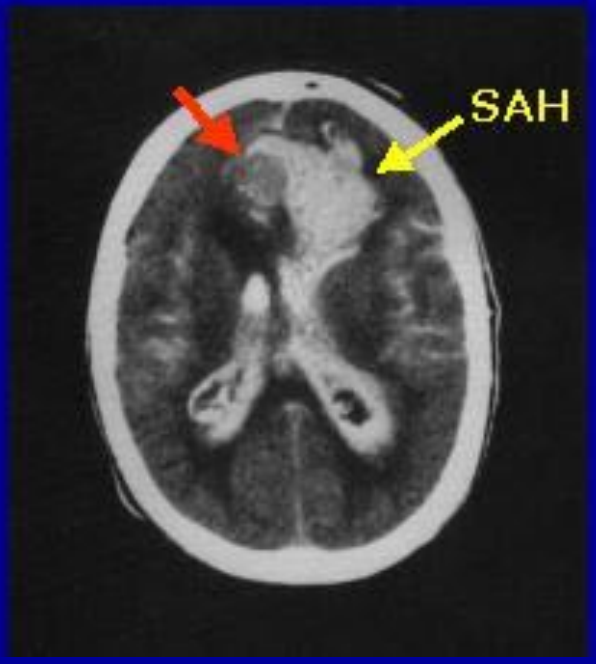
Intracranial Aneurysms and SAH





(Arrows indicate aneurysms)

Schievink, *NEJM*, 1997

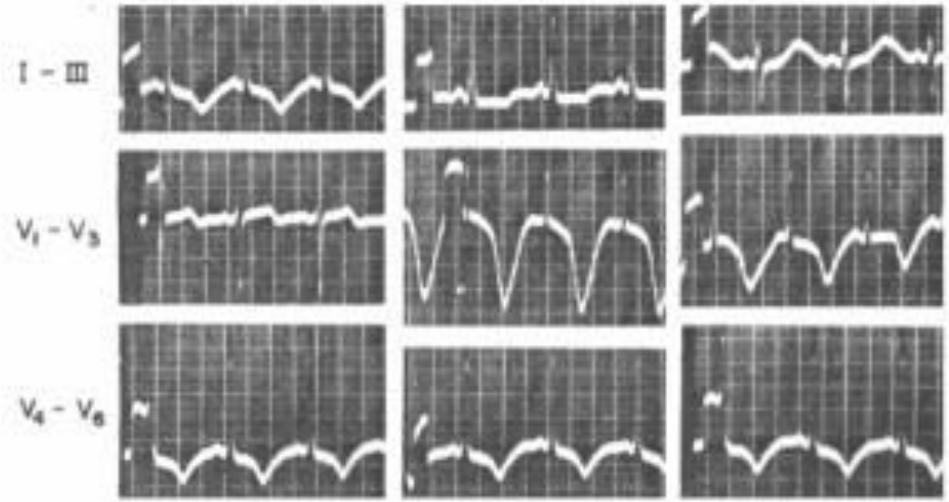
Intracranial Aneurysms and SAH

- Prevalence of intracranial aneurysms: 1 – 6% of adults
- Incidence of aneurysmal SAH: 1 / 10,000
- Risk Factors: female sex, connective tissue disorders, age, smoking, HTN
- Presentation:
  - exertion or stress
  - acute & severe headache
  - 20% pre-hospital mortality
- Complications: rebleeding, vasospasm, medical
- Therapies:
  - Surgical or embolic closure of aneurysm
  - Medical therapies for vasospasm

Schievink, *NEJM*, 1997

A New Electrocardiographic Pattern Observed in Cerebrovascular Accidents

By G. E. Burch, M.D., Robert Meyers, M.D., and J. A. Abildskov, M.D.



Circulation, 1954

Cardiac Effects of SAH

- ECG changes: 25 – 75%
- Arrhythmia: *torsade de pointes* is classic but rare
- LV dysfunction / Congestive heart failure
- CPK-MB / troponin release
- Contraction band necrosis of the myocardium
- 20% pre-hospital mortality – sudden cardiac death?

Frequency and Regional Distribution of LV Systolic Dysfunction After Subarachnoid Hemorrhage: an Echocardiographic Assessment

Jonathan G. Zaroff MD, Guy A. Rordorf MD,
Christopher S. Ogilvy MD, Michael H. Picard MD
Massachusetts General Hospital, Boston MA

Introduction

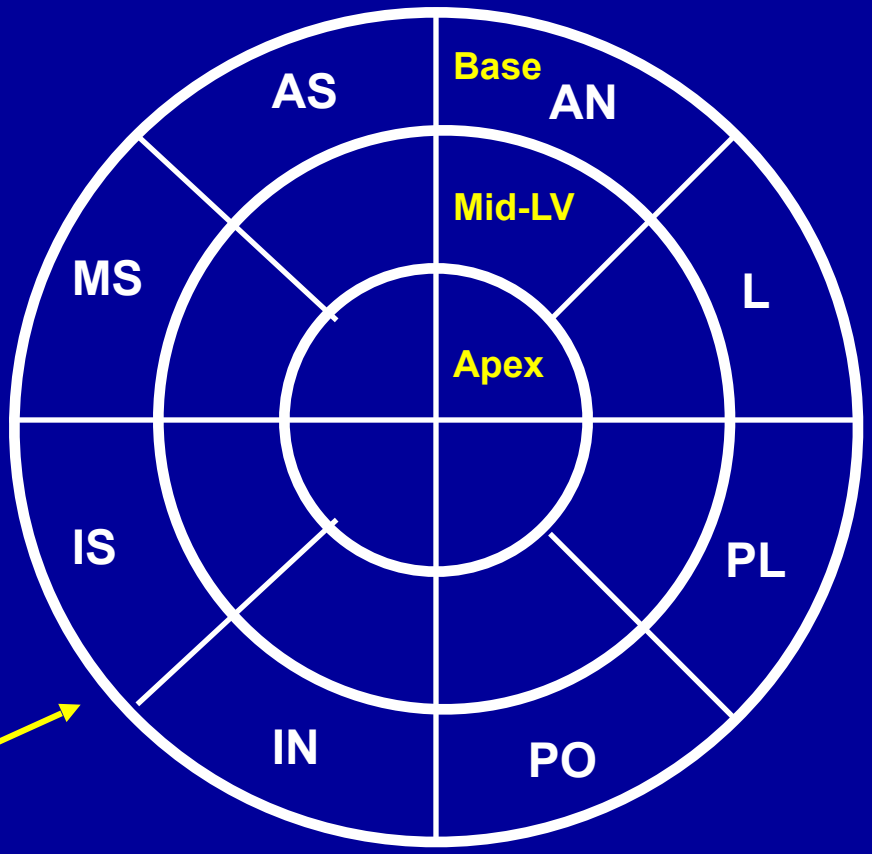
- LV dysfunction has been reported after SAH and two small studies reported an incidence of 9 - 30% (Pollick, *JACC* 1988 and Davies, *Br J Anaes* 1991)
- No large study has determined the incidence and segmental distribution of LV dysfunction after SAH and its etiology remains unknown
- The role of CAD in this syndrome must be clarified to improve care of SAH patients & increase the heart donor potential of those developing brain death

Objectives

- Determine the incidence of LV dysfunction in a large series of SAH patients referred for echocardiography
- Describe the regional patterns of LV dysfunction
- Determine whether these patterns match coronary artery distributions as seen in patients with myocardial infarction

Methods

- Clinical SAH & echolab databases
- Patients with an echo during their SAH admission were identified
- Exclusion criteria: history of CAD or cardiomyopathy
- Global LV dysfunction - diffuse hypokinesis
- Segmental dysfunction
  - hypokinesis, akinesis, or dyskinesis
  - 20 segment model



Key: AS=anteroseptal, MS=midseptal, IS=inferoseptal, IN=inferior, PO=posterior, PL=posterolateral, L=lateral, AN=anterior

Results - Patient Acquisition

589 SAH patients

↓

147 w/ ECHOs

↓

41 w/ LV Dysfunction

↓ → 11 w/hx CAD/CMP

30 patients in the study group

Zaroff et al, JASE, 2000

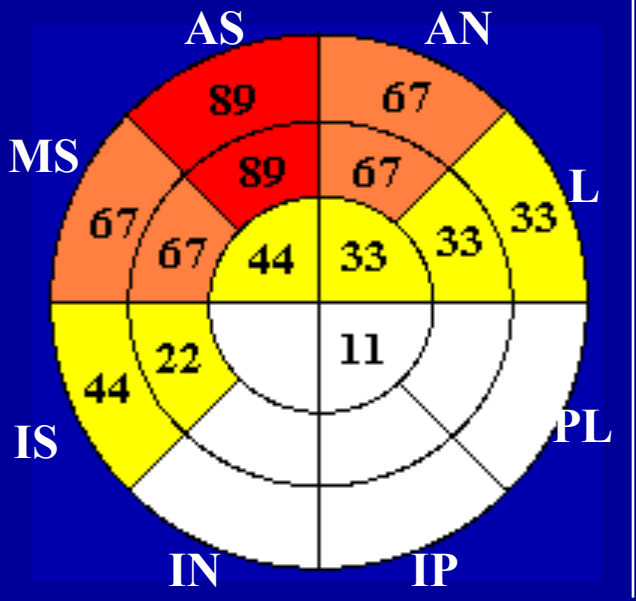
Clinical and Echocardiographic Characteristics of the Study Group (n=30)

- Age: mean 53, range 24 - 76
- 23 (77%) female
- Brain death in 8 (27%)
- 20% of SAH patients referred for echocardiography
- Indications for echo: assess LV fxn (13), CHF (6), heart donor evaluation (6), other (5)
- LV ejection fraction < 50% in 16 patients (53%)
- Global LV dysfunction - 9 patients
  - Apical function preserved in 5/9
- Segmental LV dysfunction - 21 patients
- F/up echos showed normalization of LV function in 5/6

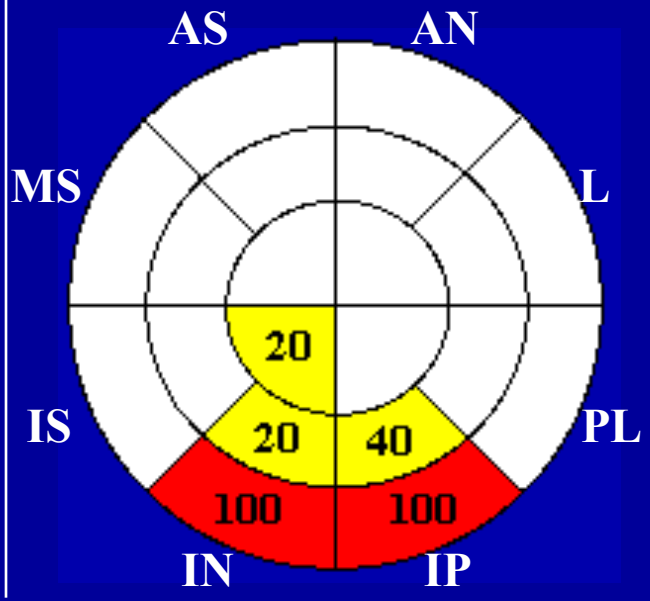
Zaroff et.al., JASE, 2000

Segmental Patterns of LV Dysfunction

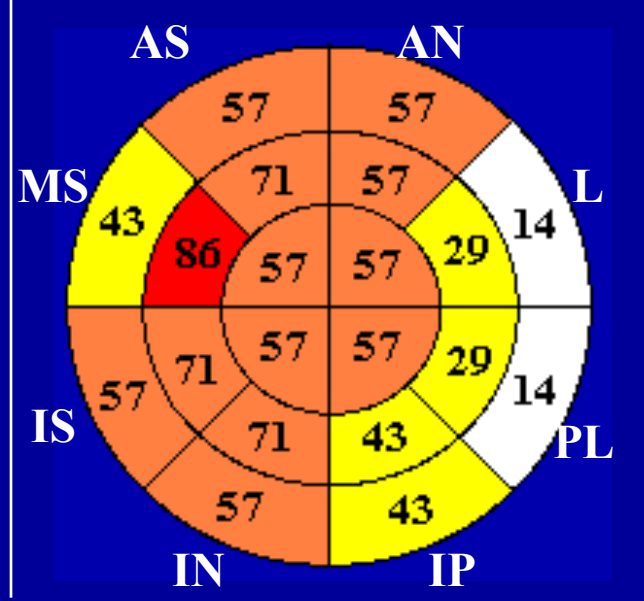
Anterior/Septal N=9



Inferior N=5



Multiple N=7



Incidence of RWMA:

- 75 - 100%
- 50 - 74%
- 20 - 49%
- 0 - 19%

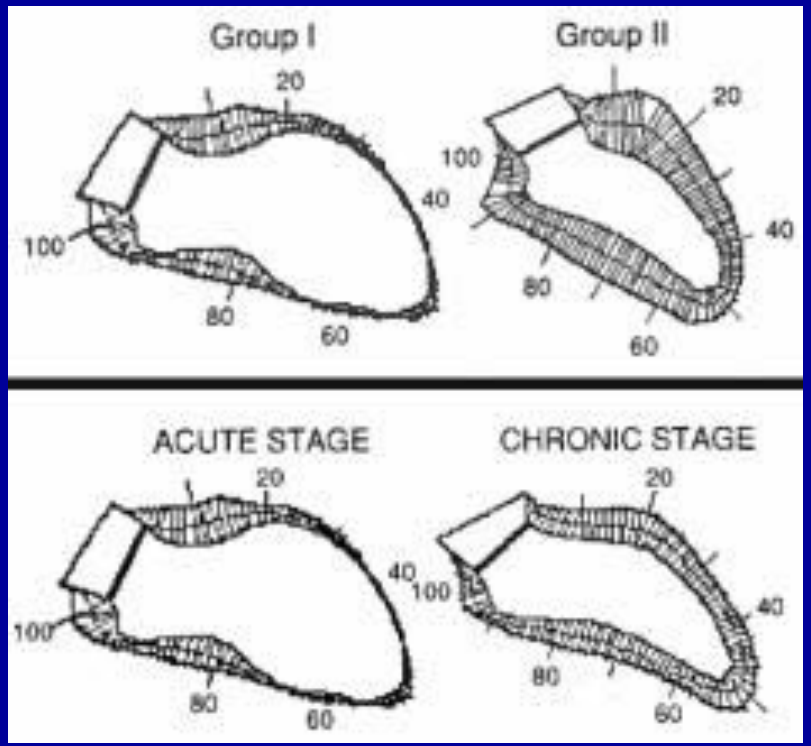
Zaroff et al, JASE, 2000

STUDY CONCLUSIONS

- LV dysfunction is common in SAH patients referred for echocardiography and occurs in patients without known CAD or cardiomyopathy

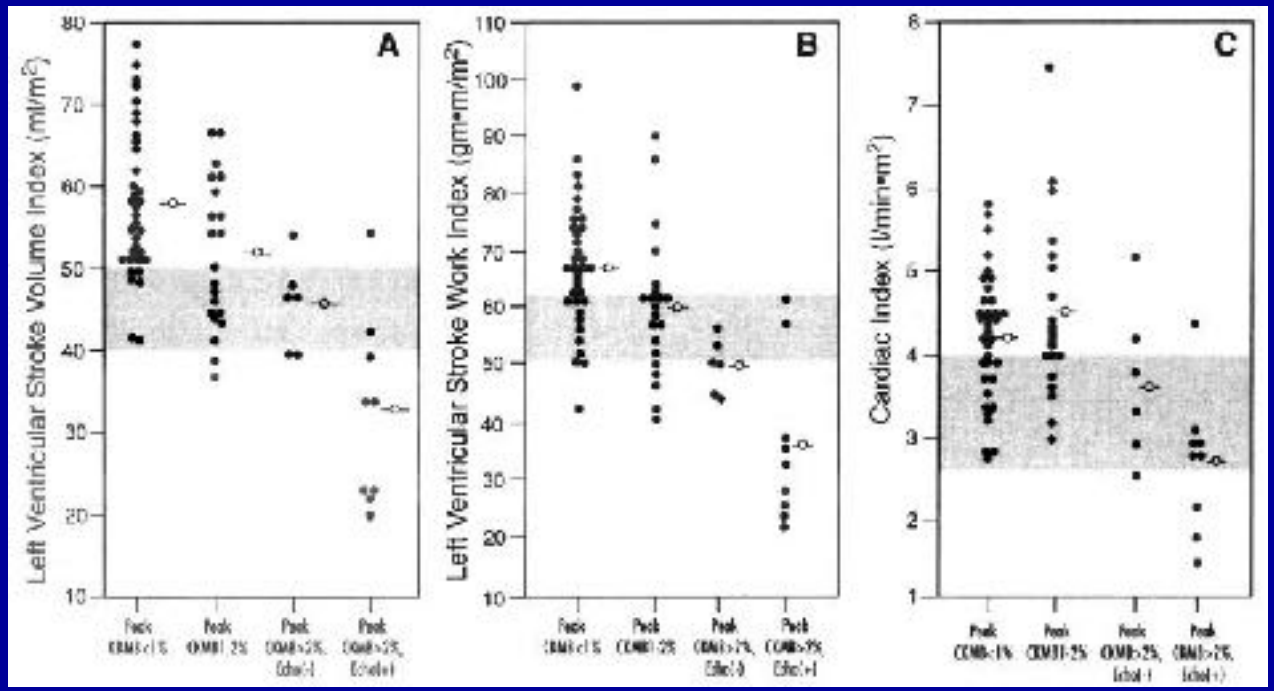
- The patterns of LV dysfunction are not c/w CAD as the dominant etiology
  - Involvement of the inferoseptum & sparing of the apex in the "anterior" pattern
  - Frequent occurrence of "multiple" territory RWMA & global dysfunction

Apical Akinesis in SAH Patients with ST Elevation & Normal Coronary Arteries



Kono et.al., JACC, 1994

Clinical Significance: CPK MB Release & LV Dysfunction Result in Cerebral Vasospasm



*Depressed cardiac index was an independent predictor of symptomatic cerebral vasospasm, a major cause of morbidity and mortality in SAH patients

Mayer et.al., Stroke, 1998

Possible Etiologies of Cardiac Dysfunction After SAH

- Coronary Artery Disease (CAD)
  - Difficult to exclude
  - Epidemiological factors argue against a primary role of CAD (SAH patients are 65% women, mean age=50 years)
- Coronary spasm – no evidence available
- Myocardial ischemia due to "supply/demand mismatch"
  - Hypertension, tachycardia, volume overload
- The Catecholamine Hypothesis
  - Supported by animal experiments
  - Difficult to prove in humans

Regional Myocardial Perfusion in Experimental Subarachnoid Hemorrhage

- Hypotheses:
  - A canine model can be developed to assess the epicardial and microvascular coronary circulation before and after SAH.
  - SAH-induced ECG changes and LV dysfunction may occur in the absence of CAD and epicardial vasospasm.

Measurements

- CPK MB: > 5 ng/ml & MB Index > 2.5%
- ECG: 1mm ST elevation, 1mm ST depression, or T wave inversion in leads without baseline abnormalities
- Hemodynamic Assessment
  - HR, SBP, LAP, PAP, C.O. (thermodilution)
- 2D ECHO
  - LV regional wall motion abnormalities (RWMA) assessed in the short-axis view at the mid-papillary level using an 8 segment model
  - RWMA defined by hypokinesis or akinesis of two contiguous segments or one segment over two contiguous time points
  - Global LV function assessed by a wall motion score: each of the eight segments graded as 1 (normal), 2 (hypokinetic), or 3 (akinetic)

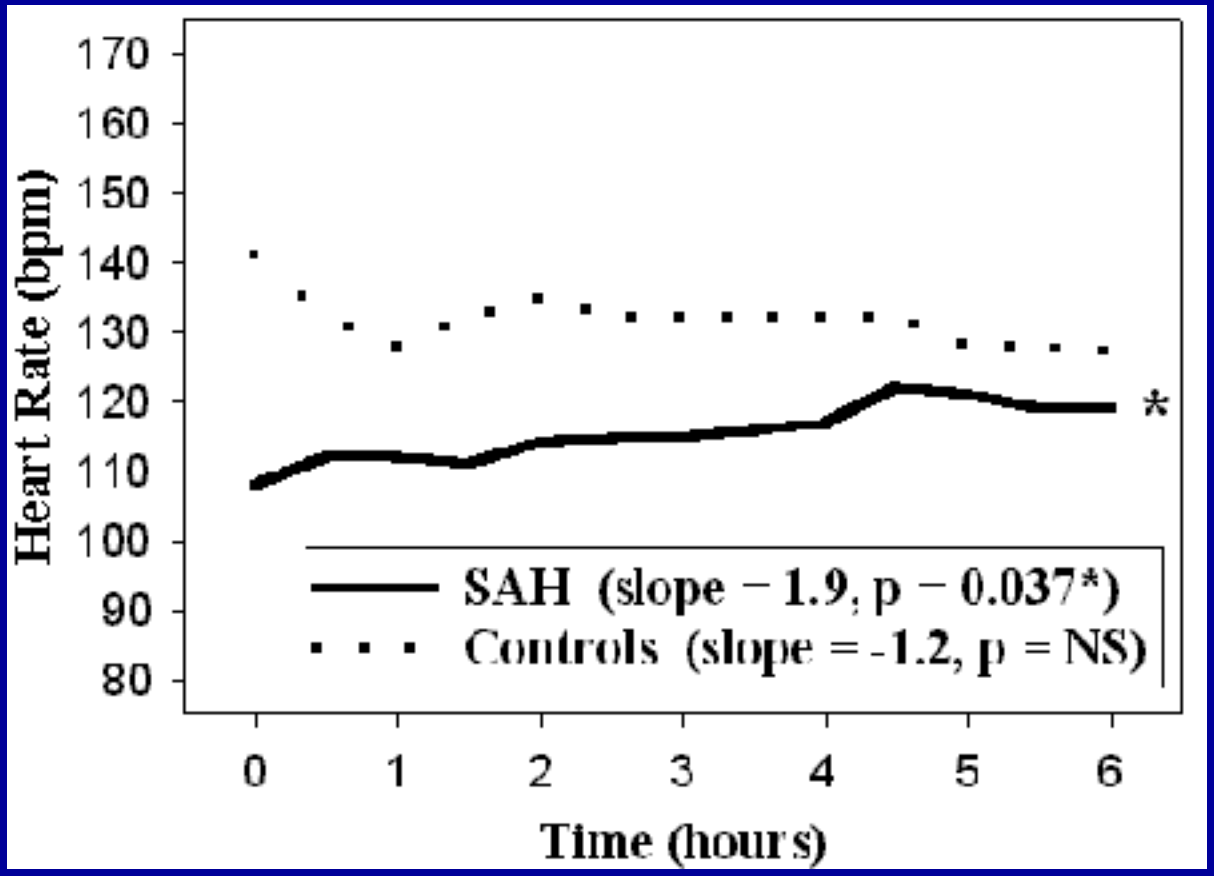
Evaluation of Myocardial Blood Flow

- Coronary angiography: Aortic root injections
- Myocardial Contrast Echocardiography (MCE)
  - Aortic root injections of Albunex^{R} or Optison^{R}
  - Epicardial imaging, triggered at end-diastole, harmonic mode
  - LV perfusion analysis at the mid-papillary level
- Radiolabeled microspheres
  - Left atrial injection of 1 - 2 million 15*u* microspheres
  - Collection at the aortic root
  - Isotopes: Ce^{141}, Sn^{113}, Ru^{103}, Nb^{95}
  - Regional myocardial blood flow determined using standard methods: 16 subendocardial and subepicardial regions at the mid-papillary level evaluated

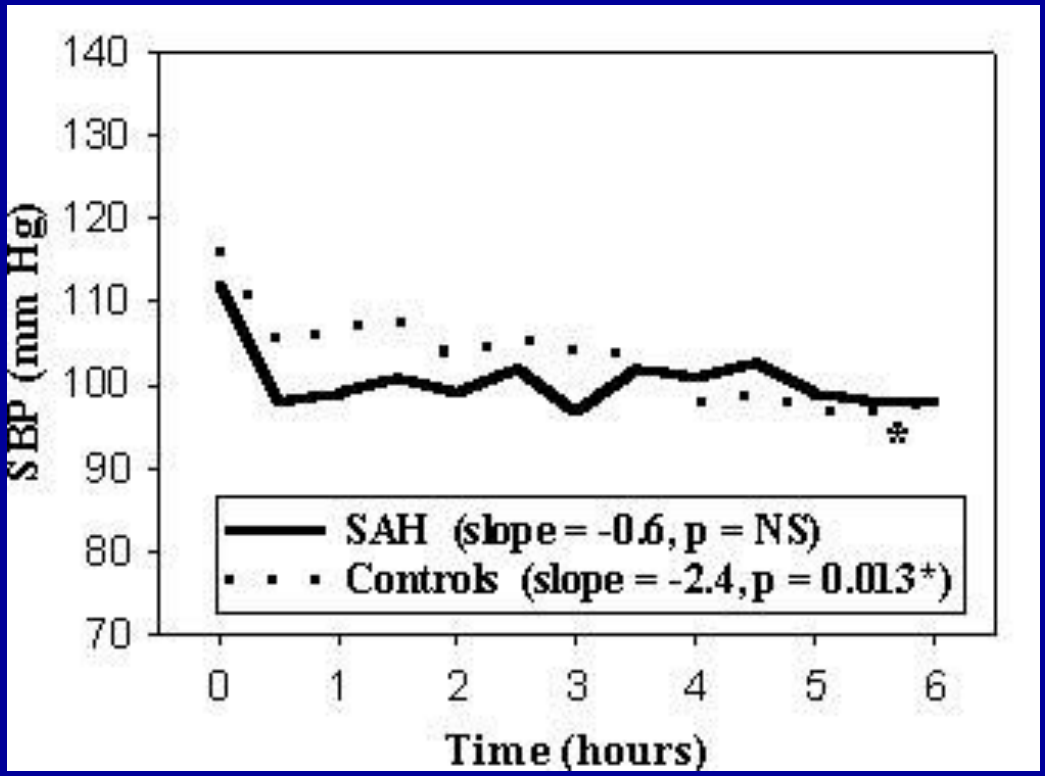
Post-SAH Evaluation

- Q30 - 60 minute monitoring of hemodynamics, ECG, ABGs, & 2D ECHO
- Repeat coronary angiography, MCE, and microspheres:
  - Repeated at 30 and 60 minutes (2 dogs)
  - Repeated at 4 - 6 hrs (all dogs)
- Euthanasia at 4-6 hrs
  - Sectioning of the LV myocardium at the mid-papillary level for:
    - pathological examination for contraction band necrosis (CBN)
    - microsphere counting/flow calculations
  - Gross pathological exam of the brain to confirm SAH

Heart Rate After SAH



Systolic Blood Pressure After SAH



Evidence of Cardiac Injury - SAH Dogs

SAH dog#	RWMA	CBN	ECG	CPK MB
1	+	+	+	-
2	+	+	-	-
3	+	+	+	-
4	+	+	-	-
5	+	-	-	-
6	+	+	-	-
7	+	-	+	-
8	-	-	-	-
9	+	+	-	-
Total	88.9%*	66.7%†‡	33.3%	0%

‡P = 0.001 (correlation between RWMA & CBN, Fisher's Z-test r = 0.75)

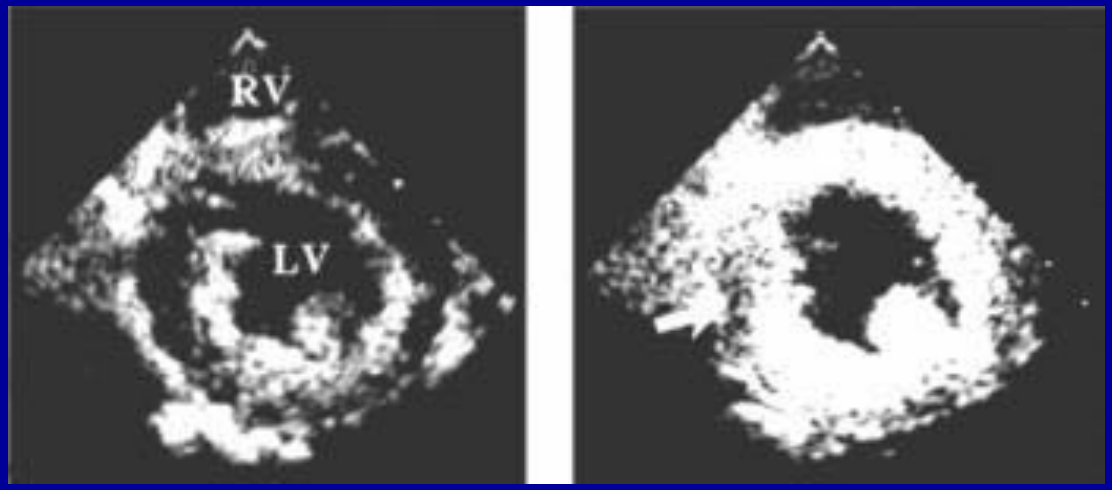
Zaroff et.al., Stroke, 2000

Results: Myocardial Blood Flow after SAH

- Coronary angiography: no evidence of vasospasm
- MCE: normal myocardial perfusion
- Radiolabeled microspheres: no effect of SAH on arteriolar blood flow

Zaroff et.al., Stroke, 2000

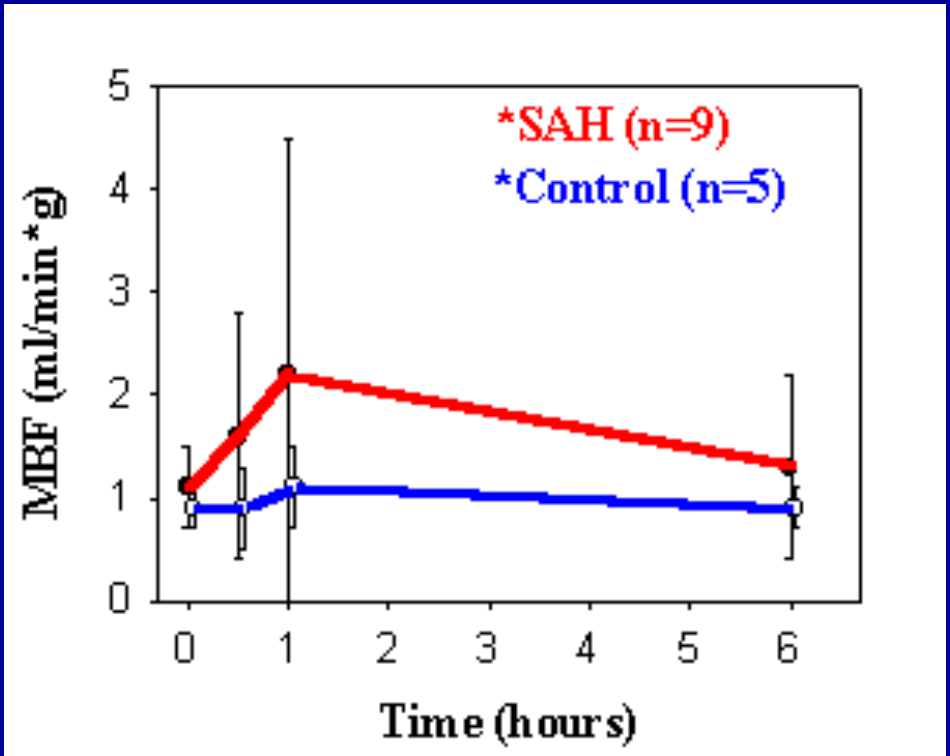
MCE Example



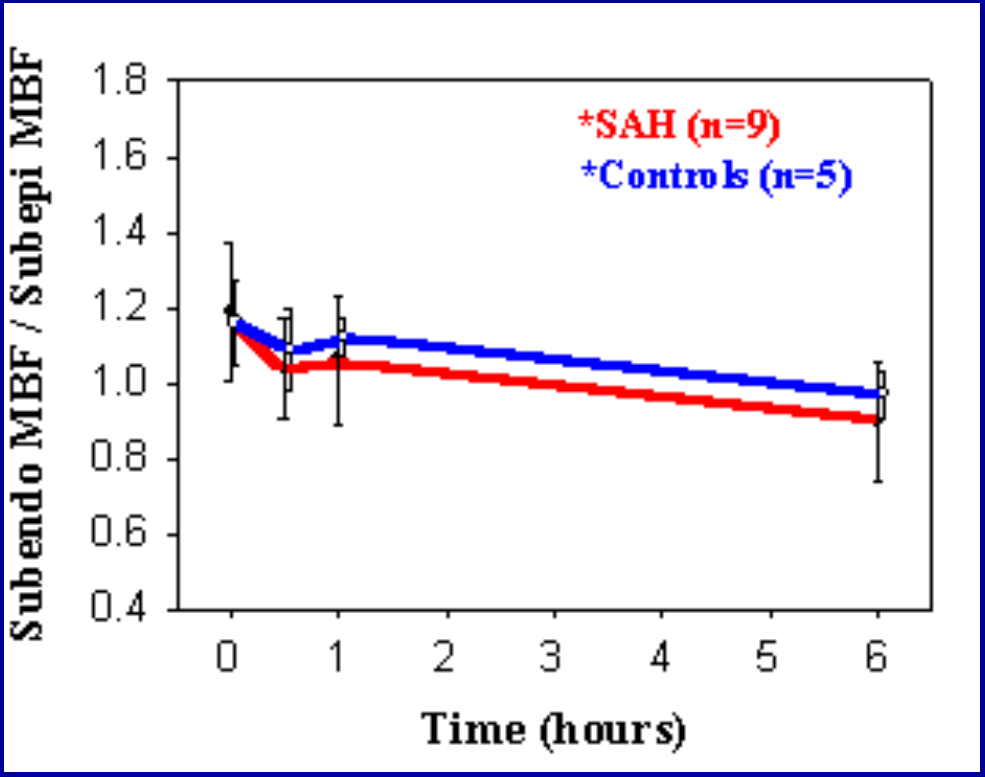
baseline MCE

Zaroff et.al., Stroke, 2000

Myocardial Blood Flow after SAH: Microsphere Data



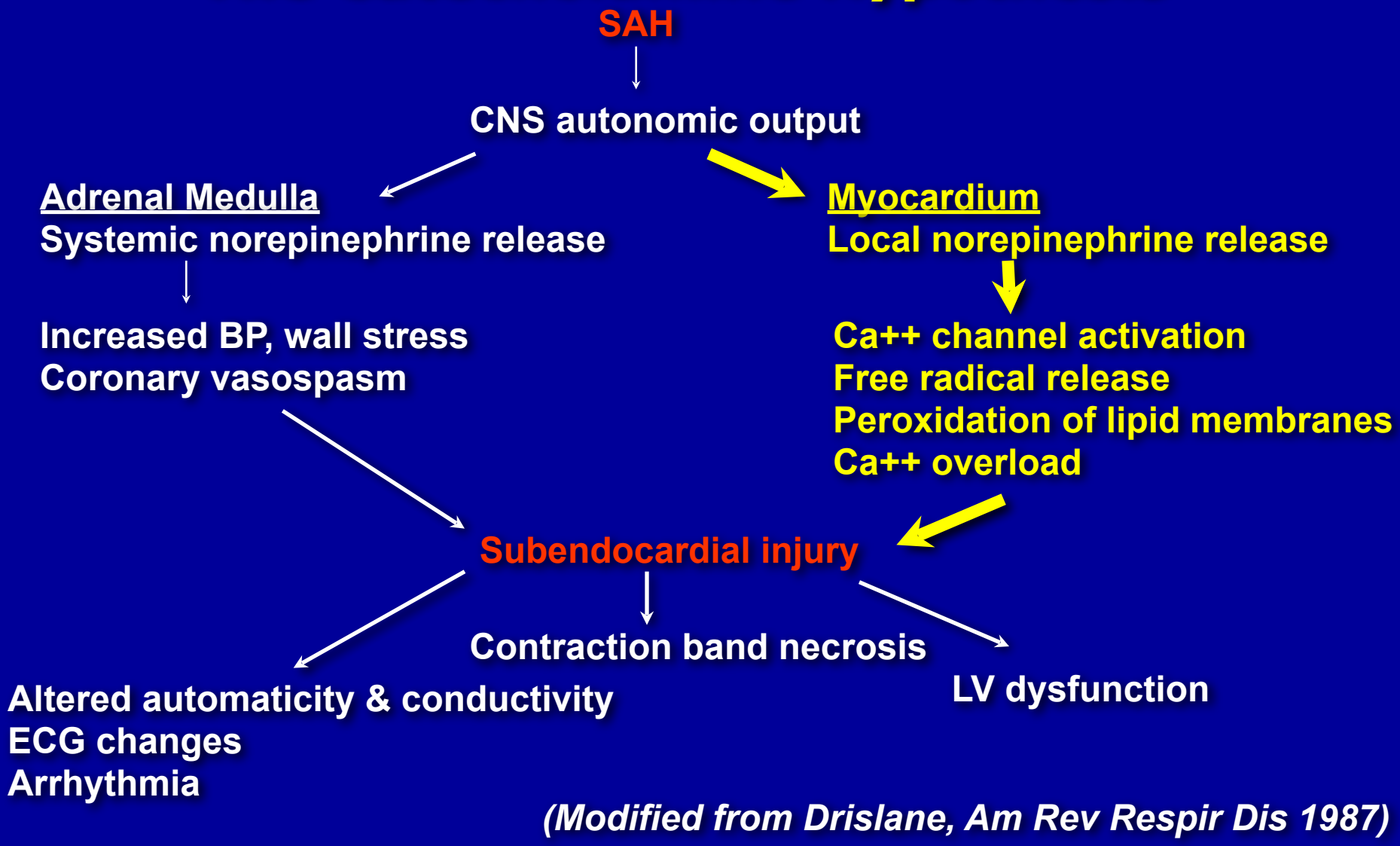
Subendocardial / Subepicardial MBF after SAH



Conclusions

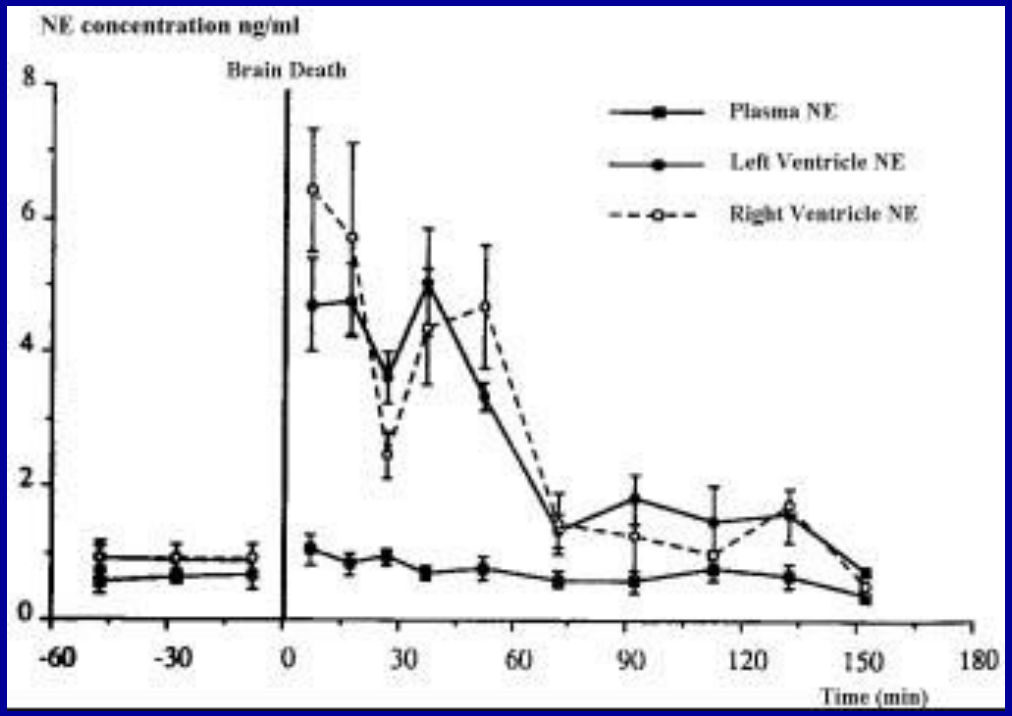
- This model reproduces the clinical and pathological cardiac lesions of SAH.
- These lesions occur in the absence of CAD, epicardial coronary spasm, and regional myocardial blood flow disturbances.

The Catecholamine Hypothesis



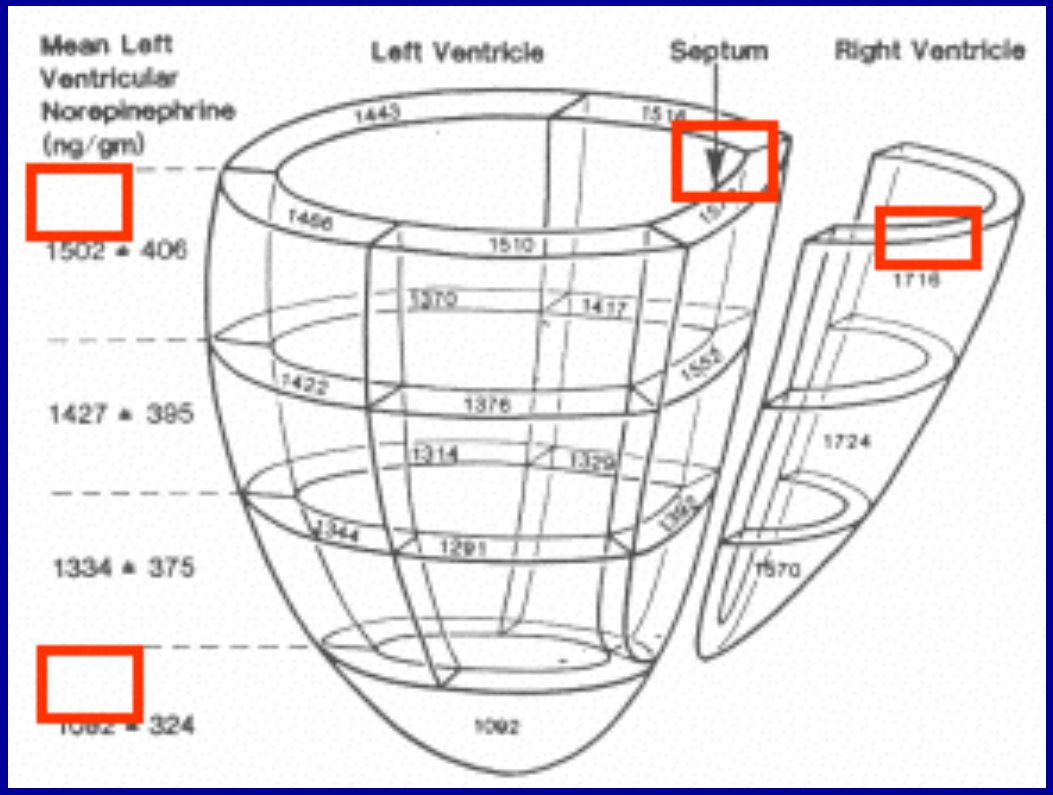
(Modified from Drislane, Am Rev Respir Dis 1987)

Myocardial Release of Norepinephrine: Experimental Evidence



Mertes, *Transplantation*, 1994

Ventricular myocardial catecholamines in primates: evidence of a relative lack of sympathetic innervation at the LV apex



From Pierpont et.al.: Ventricular myocardial catecholamines in primates, J Lab Clin Med, August 1985

Effect of Propranolol & Phentolamine on Myocardial Necrosis After SAH

- Randomized trial of 80 SAH patients
- Treatment:
  - Propranolol 80mg Q8hrs
  - Phentolamine 20 mg Q3 hrs for 3 weeks
- Results:

Group	Total #	Deaths	CBN+	ECG+
Placebo	40	6	6	6
Treatment	40	6	0	0

Neil-Dwyer, *British Medical Journal*, 1978

SAH & LV Dysfunction: Clinical Questions – Ongoing Research

- What is the true prevalence?
- Is it reversible?
- What are the relationships between ECG and wall motion patterns and the clinical/neurological status?
- What is the pathogenesis?
  - Neurally-mediated?
  - Ischemia?
  - Supply-demand mismatch?
  - Humoral factors?

CHF and SAH: The Humoral Link

Potential Mediators of Vasospasm After SAH

- Interleukin-6
- Endothelin-1
- Brain Natriuretic Peptide
- Atrial Natriuretic Peptide
- Interleukin-1 receptor antagonist
- Tumor Necrosis Factor Alpha

Management Considerations I

- A cardiotoxic milieu
  - Pressors and volume expansion
  - Therapies for CAD and CHF may be contraindicated
  - Cardiac catheterization unfeasible
- Is it CAD? Consider…
  - CAD history and risk factors
  - Time course of CPK MB release (typically prolonged without a prominent initial spike after SAH)
  - ECG patterns
  - ECHO wall motion patterns
  - Follow-up stress testing

Management Considerations II

- ICU & Perioperative Management
  - Relative sparing of pressors
  - Beta blockers
    - May prevent contraction band necrosis
    - Control of ventricular arrhythmias
  - Phentolamine, other autonomic blockers may be useful
  - Treat hypokalemia aggressively (decreases the risk of torsade de pointes)
  - Pulmonary artery catheterization if CHF occurs
- Neurological status >> cardiac status in decision making
  - ECG changes indicate neurological and not cardiac risk
  - LV dysfunction may improve with neurological recovery