



# Analysis of Stroke Occurring in the First Year of the SYNTAX Trial

Michael J. Mack MD

Heart Hospital Baylor Plano, Dallas TX

On behalf of the SYNTAX investigators

September 22, 2009

11:45am–11:57am

Moscone Center, Room 131

# Conflict of Interest Disclosure



- Steering Committee SYNTAX Trial
  - Travel Expenses Paid for Committee Meetings

## Risk of Stroke

- Neurological deficit > 72 hours
- In hospital/ 30 days

## CABG

- STS Database 2002–2006, n= 774,881
- Stroke = **1.4%**

## PCI

- NCDR Database, 2004–2007, n=706,782
- Stroke = **0.22 %**

# Objectives



- Assess the stroke rate in SYNTAX
- Define risk factors and outcomes of patients who experience a stroke in the trial

# Stroke Protocol Definitions



## **TRANSIENT ISCHEMIC ATTACK (TIA)**

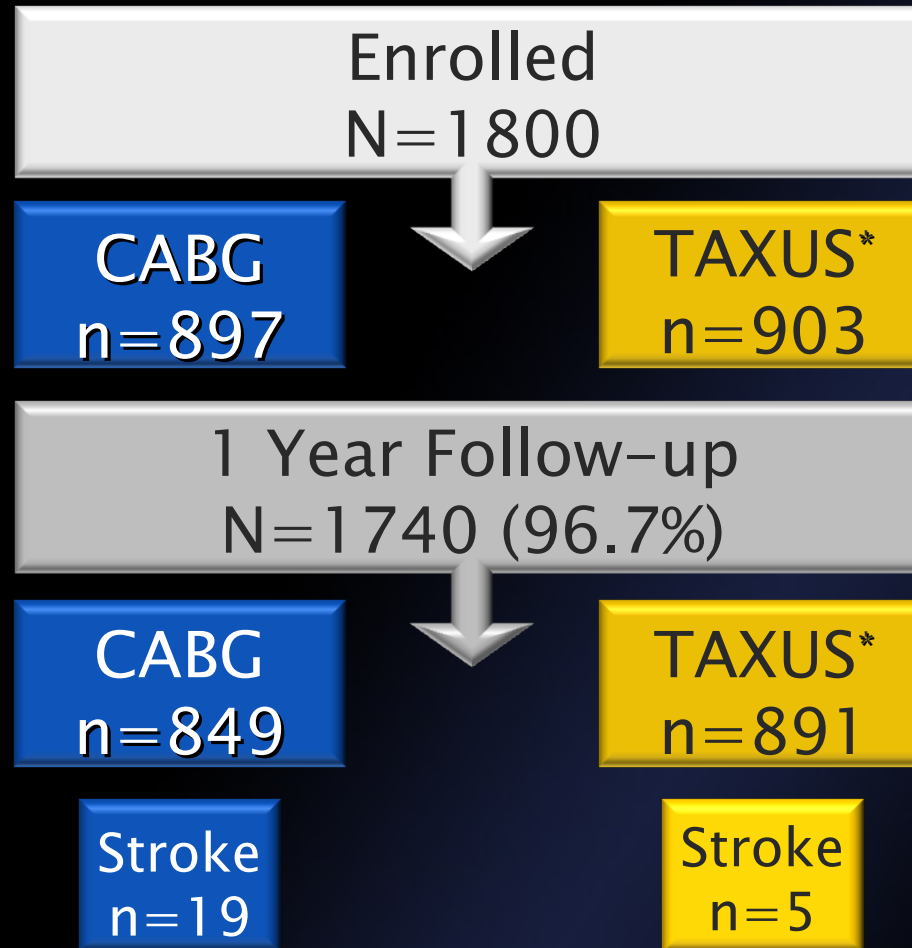
- Focal neurological deficit <24 hours

## **CEREBROVASCULAR EVENT (CVA)**

- A focal neurological deficit >72 hours with irreversible brain damage or permanent impairment
- Classified as ischemic or hemorrhagic
- Per protocol: *“CVA will be confirmed by a local neurologist”*
- Adjudicated by the CEC (including a neurologist)

# Patients with Stroke in SYNTAX

*Randomized Cohort, Intent-to-Treat*



\*TAXUS Express

# Baseline Patient Characteristics (I)

## *Potential Risk Factors for Stroke*



	CABG N=897	TAXUS N=903	P value
Age, mean $\pm$ SD (y)	65.0 $\pm$ 10.0	65.2 $\pm$ 10.0	0.55
Male, %	78.9	76.4	0.20
Body mass index, mean $\pm$ SD	27.9 $\pm$ 4.5	28.1 $\pm$ 4.8	0.37
Medically treated diabetes, %	24.6	25.6	0.64
Metabolic syndrome, %	45.5	46.0	0.86
Carotid artery disease, %	8.4	8.1	0.83
Peripheral artery disease, %	10.6	9.1	0.28
Prior stroke, %	4.8	3.9	0.33
Prior TIA, %	5.1	4.3	0.46
Creatinine >200 micromol/L	1.8	1.1	0.23

# Baseline Patient Characteristics (II)

## *Potential Risk Factors for Stroke*



	CABG N=897	TAXUS N=903	P value
Hypertension, %	77.0	74.0	0.14
Hyperlipidemia, %	77.2	78.7	0.44
Current smoker, %	22.0	18.5	0.06
Prior MI, %	33.8	31.9	0.39
Unstable angina, %	28.0	28.9	0.66
Congestive heart failure, %	5.3	4.0	0.18
COPD, %	9.3	7.9	0.29
Poor LVEF, %	2.5	1.3	0.08
Three-vessel disease, %	61.2	60.5	0.76
Additive euroSCORE, mean±SD	3.8 ± 4.4	3.8 ± 2.6	0.78
SYNTAX Score, mean±SD*	29.1 ± 11.4	28.4 ± 11.5	0.19



# Procedural Characteristics

## Potential Risk Factors for Stroke



	CABG N=897	TAXUS N=903	P value
Urgent Procedure, %	3.8	4.1	0.72
Emergent Procedure, %	3.9	1.8	0.007
Time to procedure, <sup>†</sup> d, mean ± SD	17.4 ± 28.0	6.9 ± 13.0	<0.001
Off-pump surgery %	15.0	--	--

	Off Pump	On Pump	P value
Stroke	1 / 134 (0.7%)	18 / 763 (2.3%)	ns

# Medications

## Potential Risk Factors for Stroke



	CABG N=897	TAXUS N=903	P value
<i>Pre/periprocedural Medication</i>			
Aspirin, %	34.9	96.9	<0.001
Heparin (unfractionated), %	40.2	84.5	<0.001
Heparin (low molecular weight), %	10.8	9.5	0.36
Bivalirudin, %	0.1	7.1	<0.001
Thienopyridine, %	1.6	97.5	<0.001
Aprotinin, %	36.7	--	--
<i>Medication at Discharge</i>			
Aspirin, %	88.5	96.3	<0.001
Thienopyridine, %	19.5	96.8	<0.001
Coumadin, %	7.1	2.6	<0.001
Statin, %	74.5	86.7	0.57

Site-reported data

# Medications at 12 Months

## *Potential Risk Factors for Stroke*



	CABG N=897	TAXUS N=903	P value
Aspirin, %	84.3	91.2	<0.001
Statin, %	81.6	85.5	0.03
Beta blockers, %	76.4	78.7	0.26
ACE inhibitors, %	51.0	51.0	0.97
Thienopyridines, %	15.0	71.1	<0.001
Diuretics, %	27.4	25.6	0.39
Calcium channel blockers, %	18.9	25.5	0.001
Angiotensin II receptor antagonists, %	13.5	19.0	0.002
Nitrates	7.5	17.4	<0.001
Oral antidiabetic, non insulin-sensitizer, %	11.1	10.3	0.61
H2-receptor blockers, %	10.7	12.2	0.35

Medications taken by  $\geq 10\%$  of patients in either group.

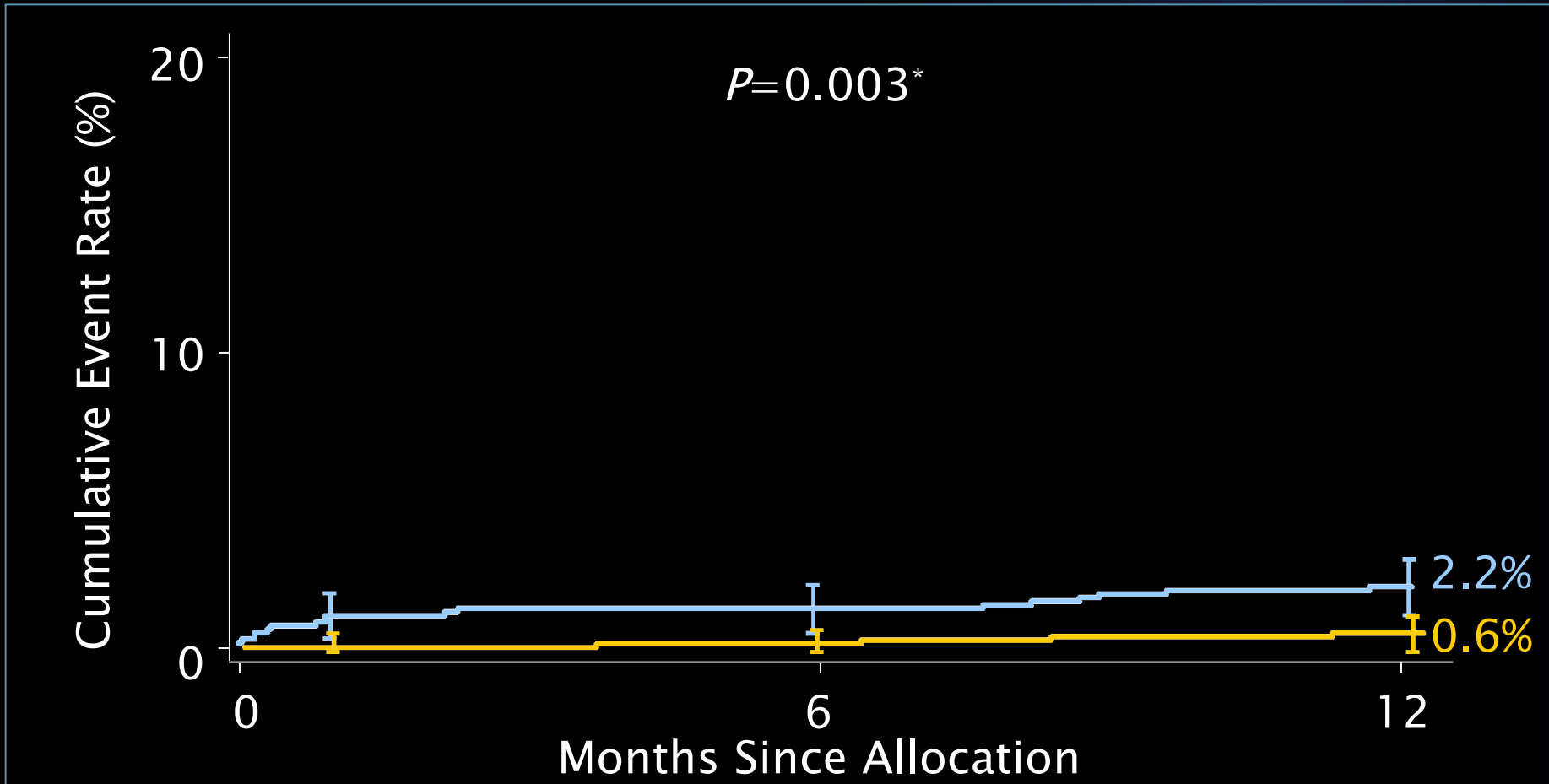
Site-reported data

# CVA (Stroke) to 12 Months



■ CABG (N=897)

■ TAXUS (N=903)



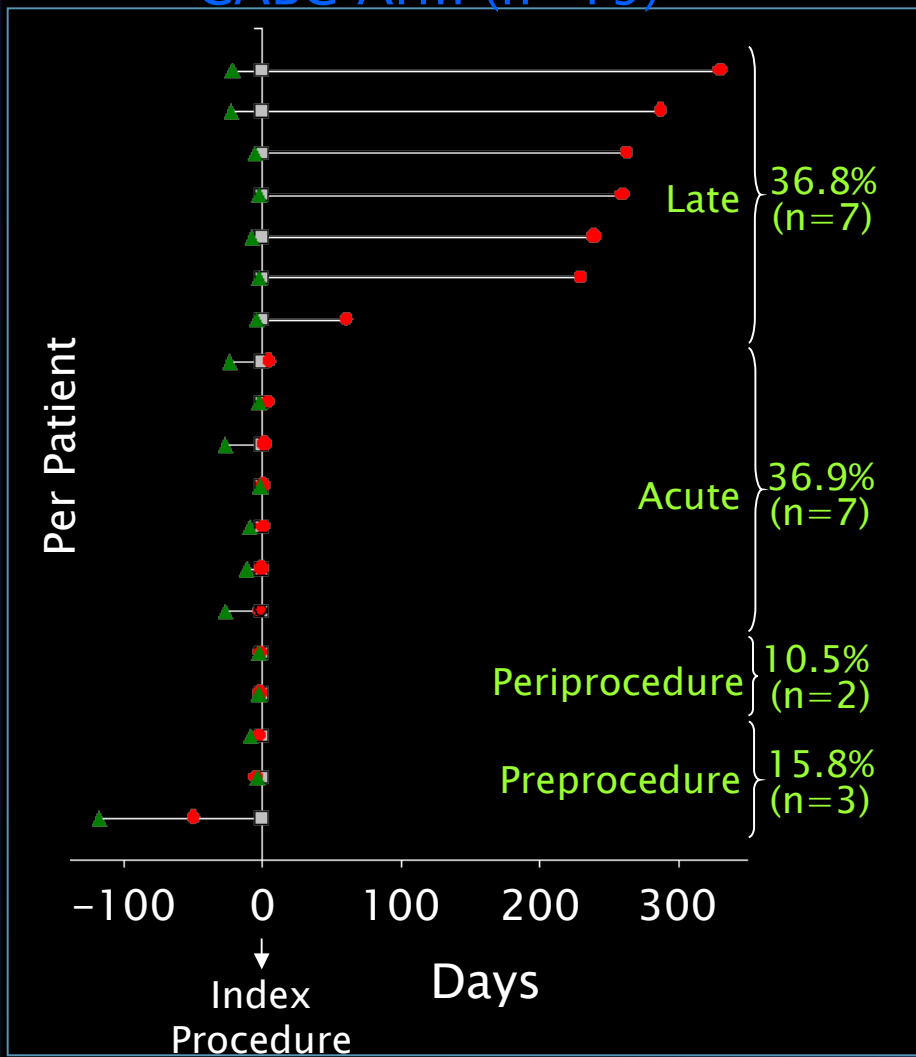
Event rate  $\pm$  1.5 SE. \*Fisher exact test

ITT population

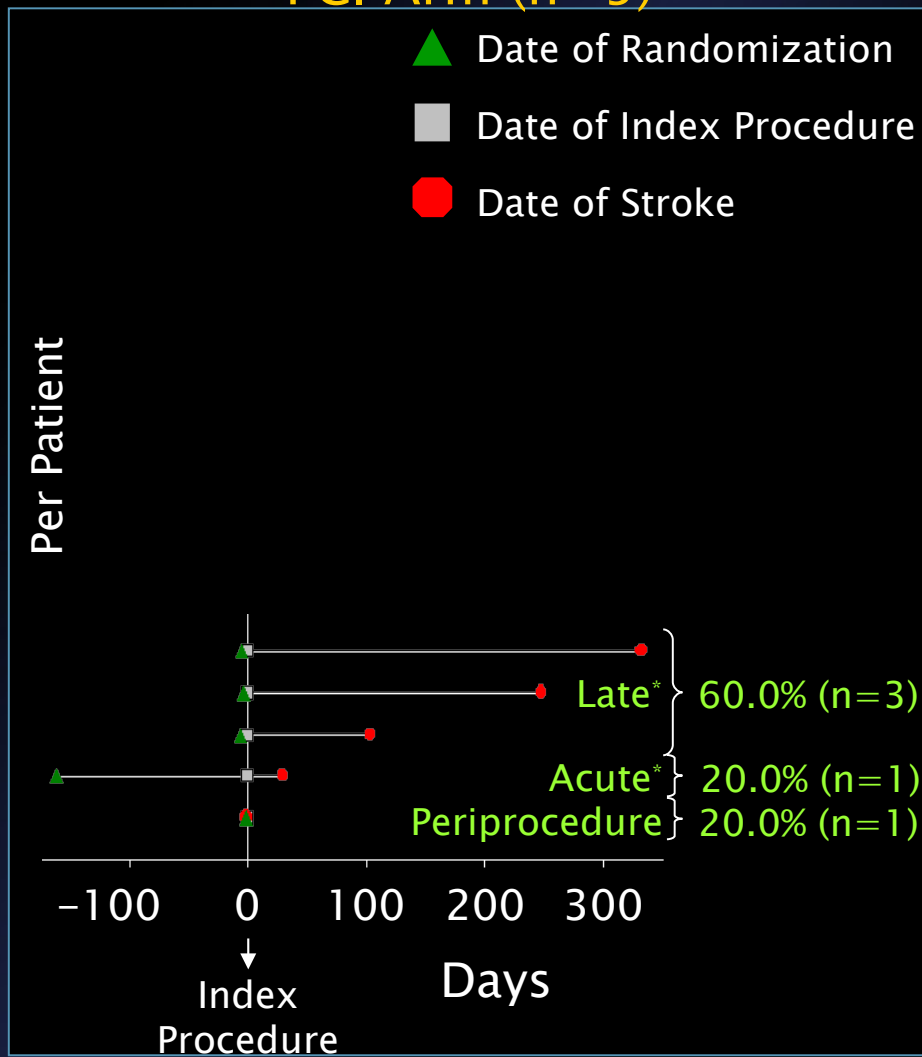
# Timing of Stroke (Per Patient)



## CABG Arm (n=19)



## PCI Arm (n=5)



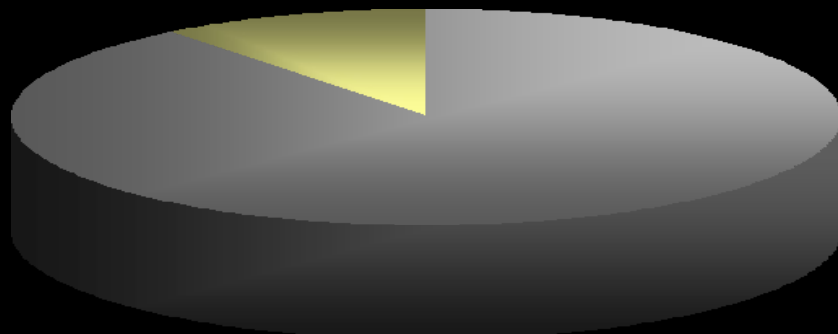
\*Late: >30days; Acute: postprocedure to ≤30d

# Type of Stroke

**CABG**  
(n=19)

Hemorrhagic  
10.5% (n=2)

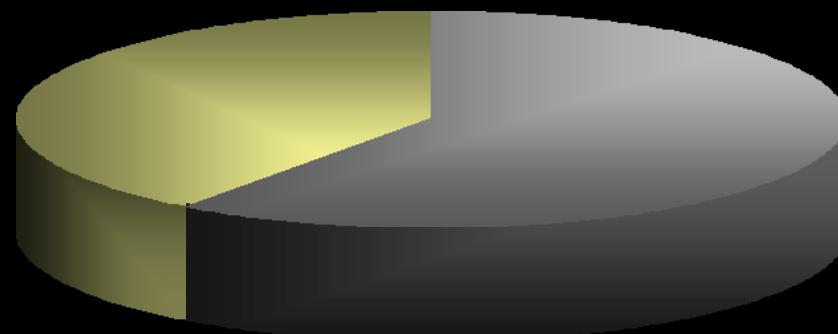
Ischemic  
89.5% (n=17)



**PCI**  
(n=5)

Hemorrhagic  
40.0% (n=2)

Ischemic  
60.0% (n=3)

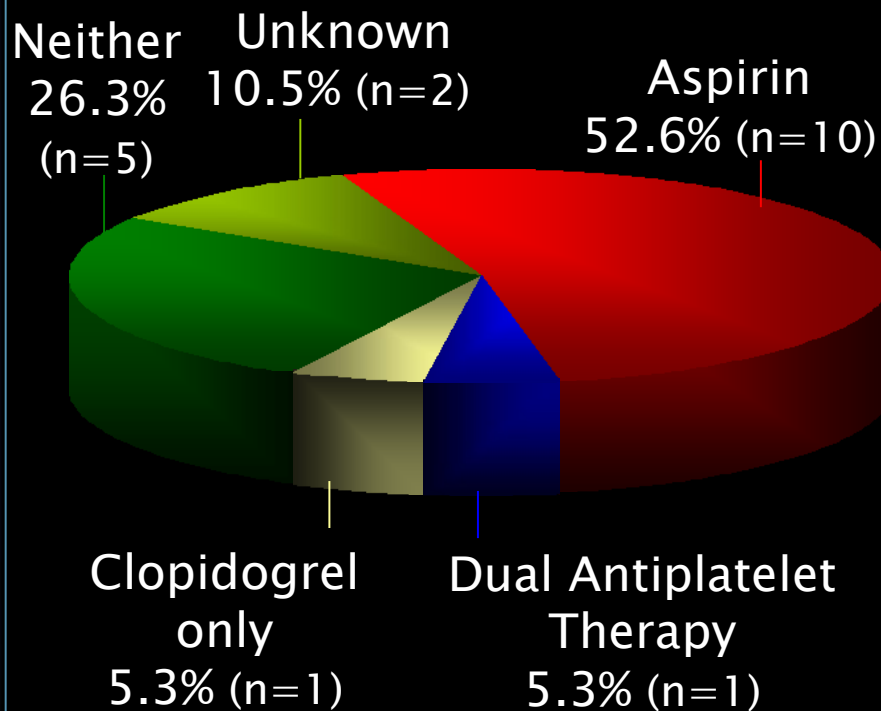


Hemorrhagic Strokes with CABG  
1- 7 days post randomization-never had CABG  
2- Fatal at home 241 days postoperatively

# Antiplatelet Therapy Status at Time of Stroke (Per Patient)

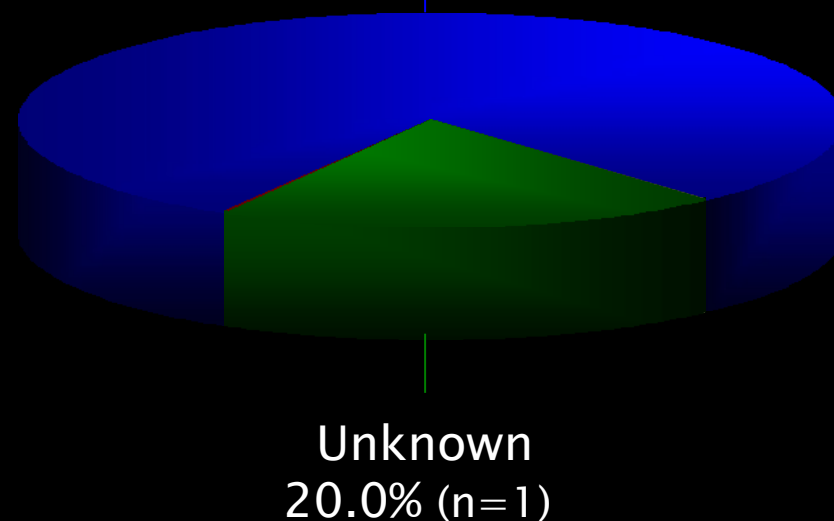


## CABG (n=19)



## PCI (n=5)

Dual Antiplatelet  
Therapy  
80.0% (n=4)



# Adverse Cardiac Events to 12 Months



## CABG (n=19)

- 6 patients
  - atrial fibrillation
    - 1 patient ST elevation MI
    - 2 patients, AF possibly led to the stroke
- 13 –no adverse cardiac events

## PCI (n=5)

- 3 patients
  - cardiac failure
  - angina
  - ST+MI
- 2 –no adverse cardiac events

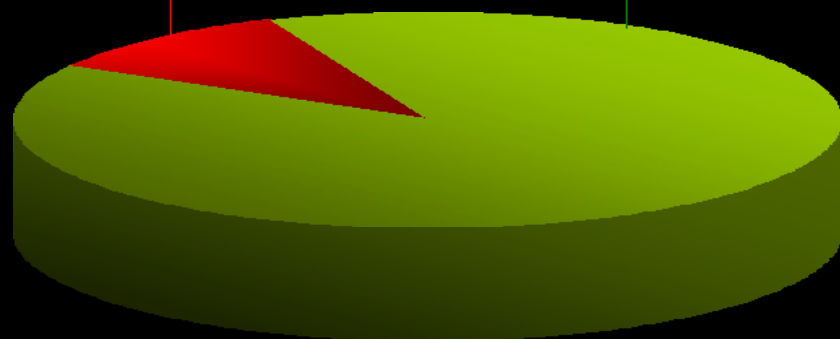


# Outcomes Following Stroke (Per Patient)

**CABG**  
(n=19)

Death  
10.5% (n=2)

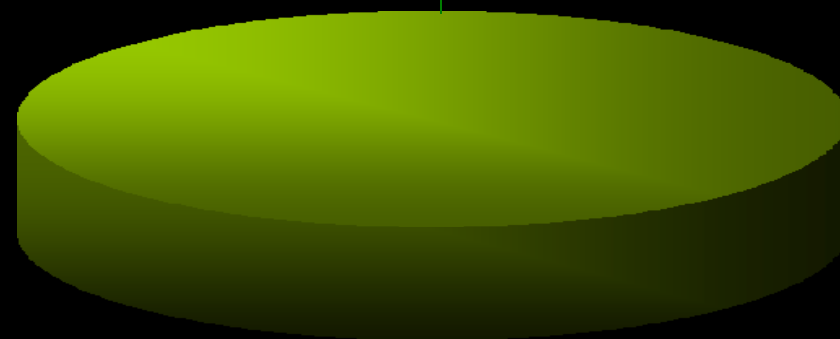
Non-fatal stroke  
89.5% (n=17)



1 death never received CABG  
4 strokes resolved without deficit

**PCI**  
(n=5)

Non-fatal stroke  
100% (n=5)



2 strokes resolved without deficit

# CVA to 12 Months by SYNTAX Score Tercile

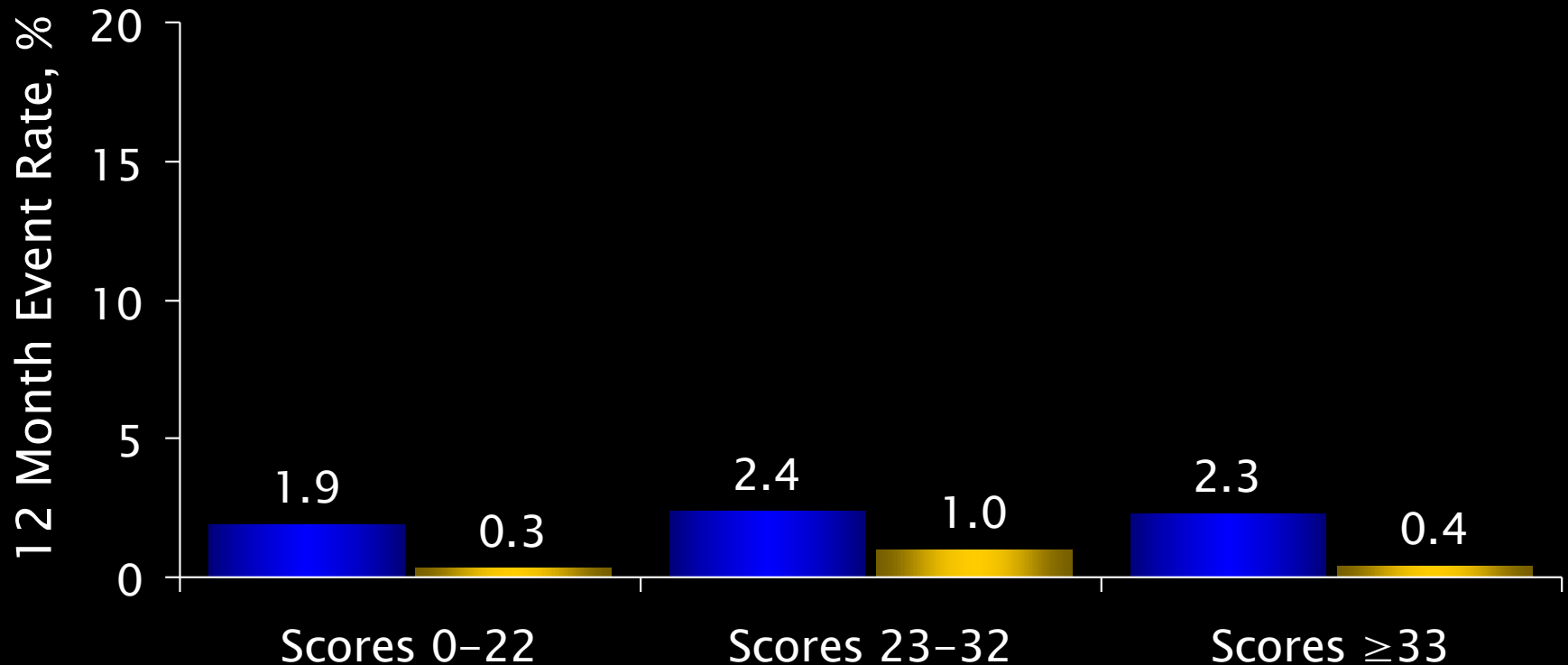


CABG TAXUS

$P=0.10$

$P=0.21$

$P=0.07$

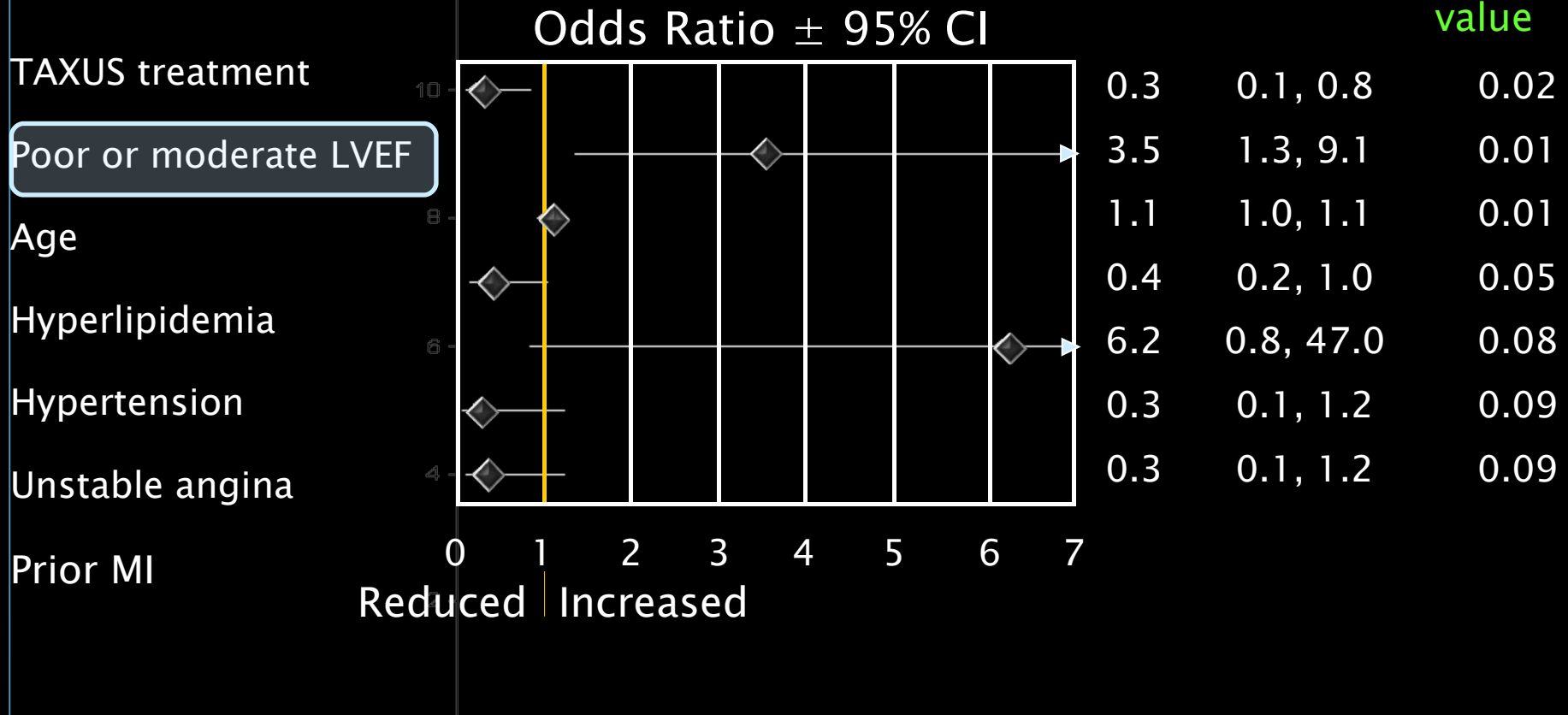


# Periprocedural Multivariate Predictors of Stroke at 12 Months

## Overall Predictors



Overall predictors (n=1800)



\*TAXUS Express

# Periprocedural Multivariate Predictors of Stroke at 12 Months

## *Predictors by Treatment Arm*



CABG (n=897)

Poor or moderate LVFF

Prior MI

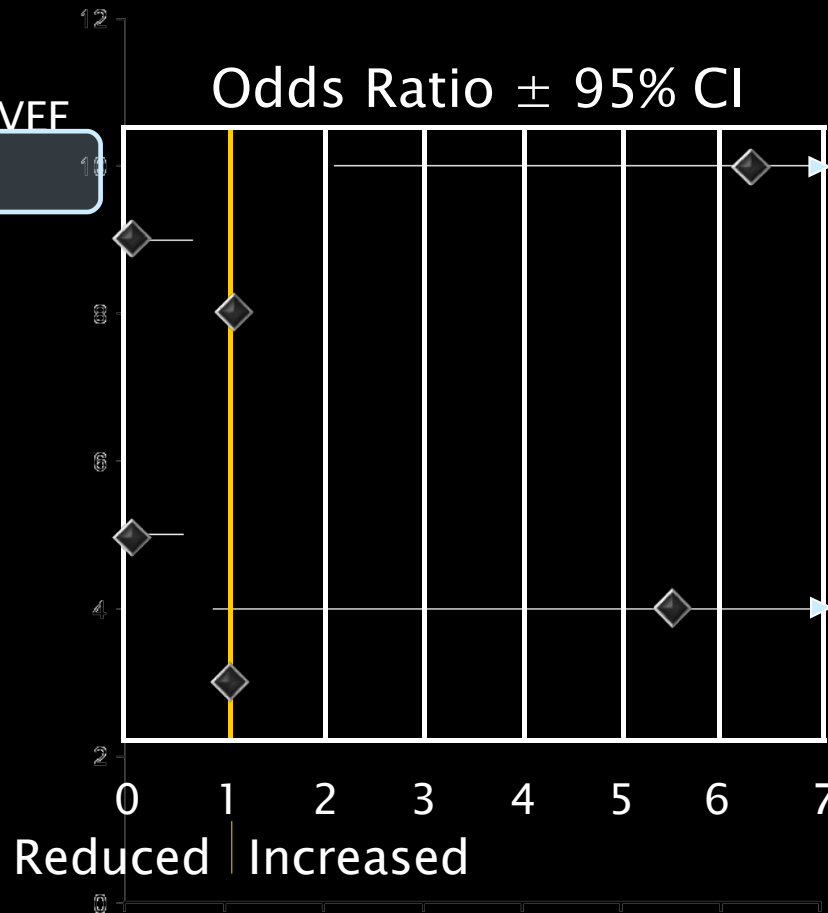
Age

TAXUS (n=903)

Hyperlipidemia

Female

Time to treatment



OR

95% CI

P value

6.3

2.1, 18.4

<0.001

0.1

0, 0.1

0.02

1.1

1.0, 1.1

0.06

0.1

0.1, 0.6

0.01

5.5

0.9, 33.7

0.09

1.0

1.0, 1.1

0.001

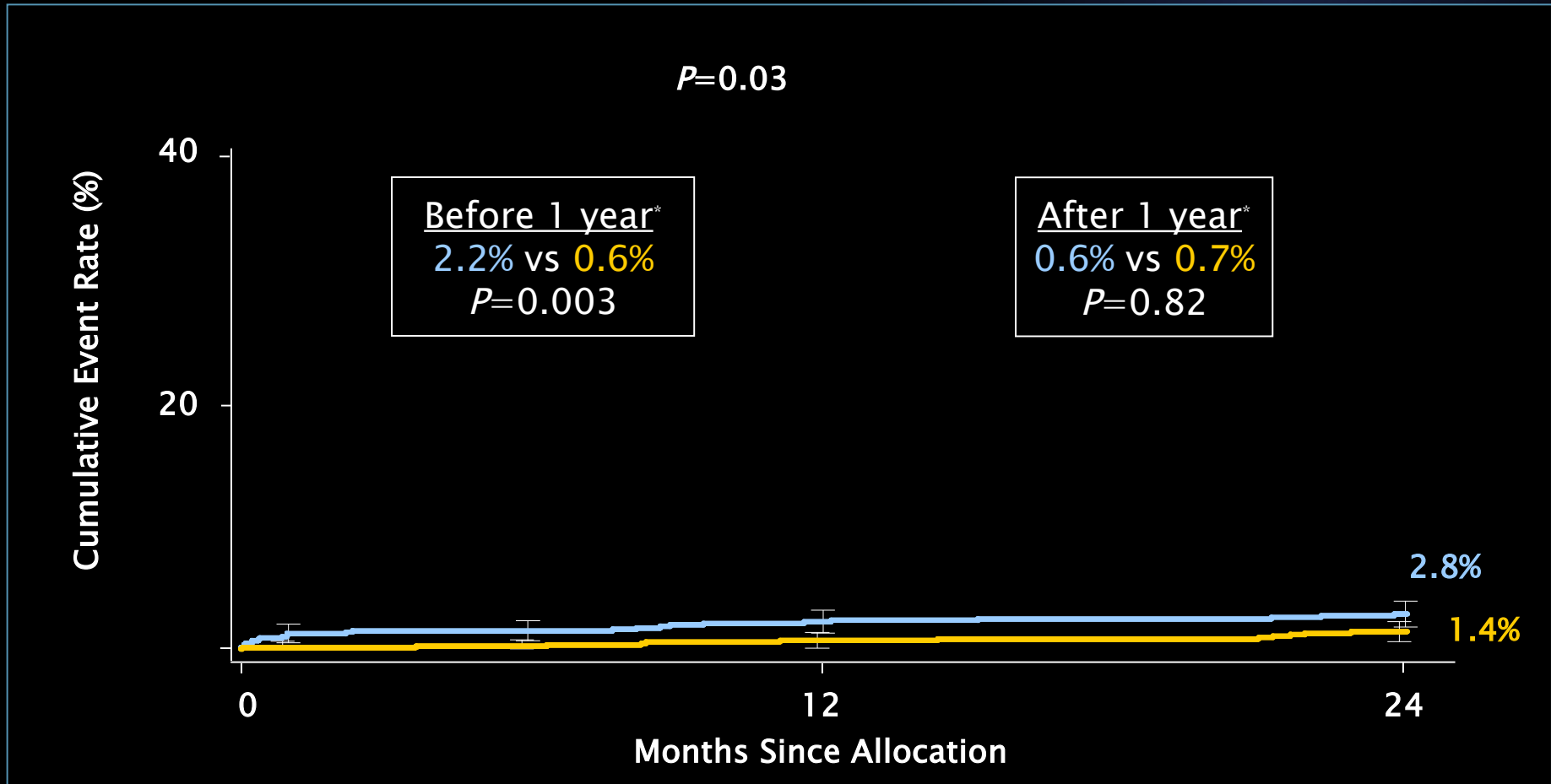
\*TAXUS Express

# CVA to 2 Years



■ CABG (N=897)

■ TAXUS (N=903)



Cumulative KM Event Rate  $\pm$  1.5 SE; log-rank  $P$  value; \*Binary rates

ITT population

# Summary



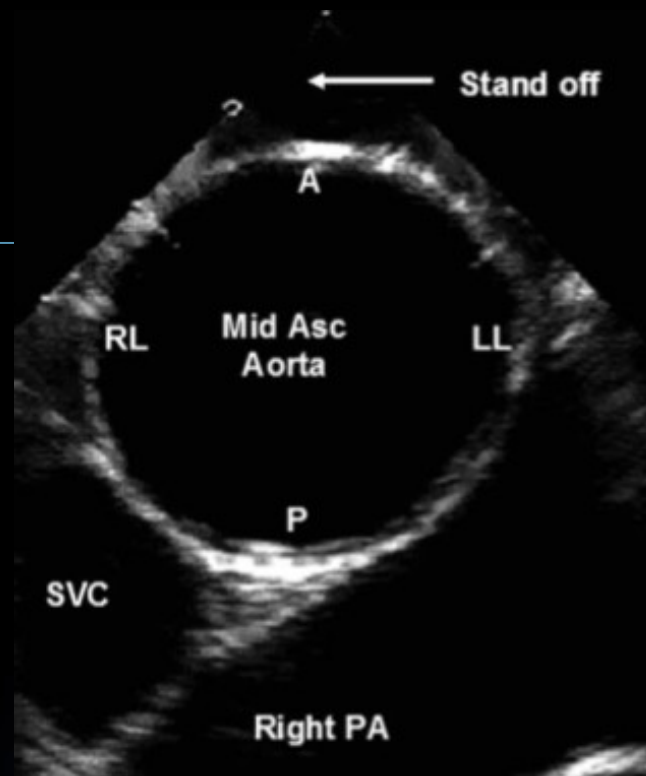
- The overall incidence of stroke was low at 1 year in the SYNTAX trial
  - Significantly more strokes in the CABG arm (n=19) versus the TAXUS arm (n=5)
  - Significantly more TAXUS patients received pre- and peri-procedural antiplatelet therapy
  - Greater proportion of peri-procedural/acute stroke in the CABG arm than TAXUS
- Majority of strokes were ischemic
- Poor or moderate LVEF was the strongest predictor and increased the risk of stroke significantly

# To My Surgical Colleagues

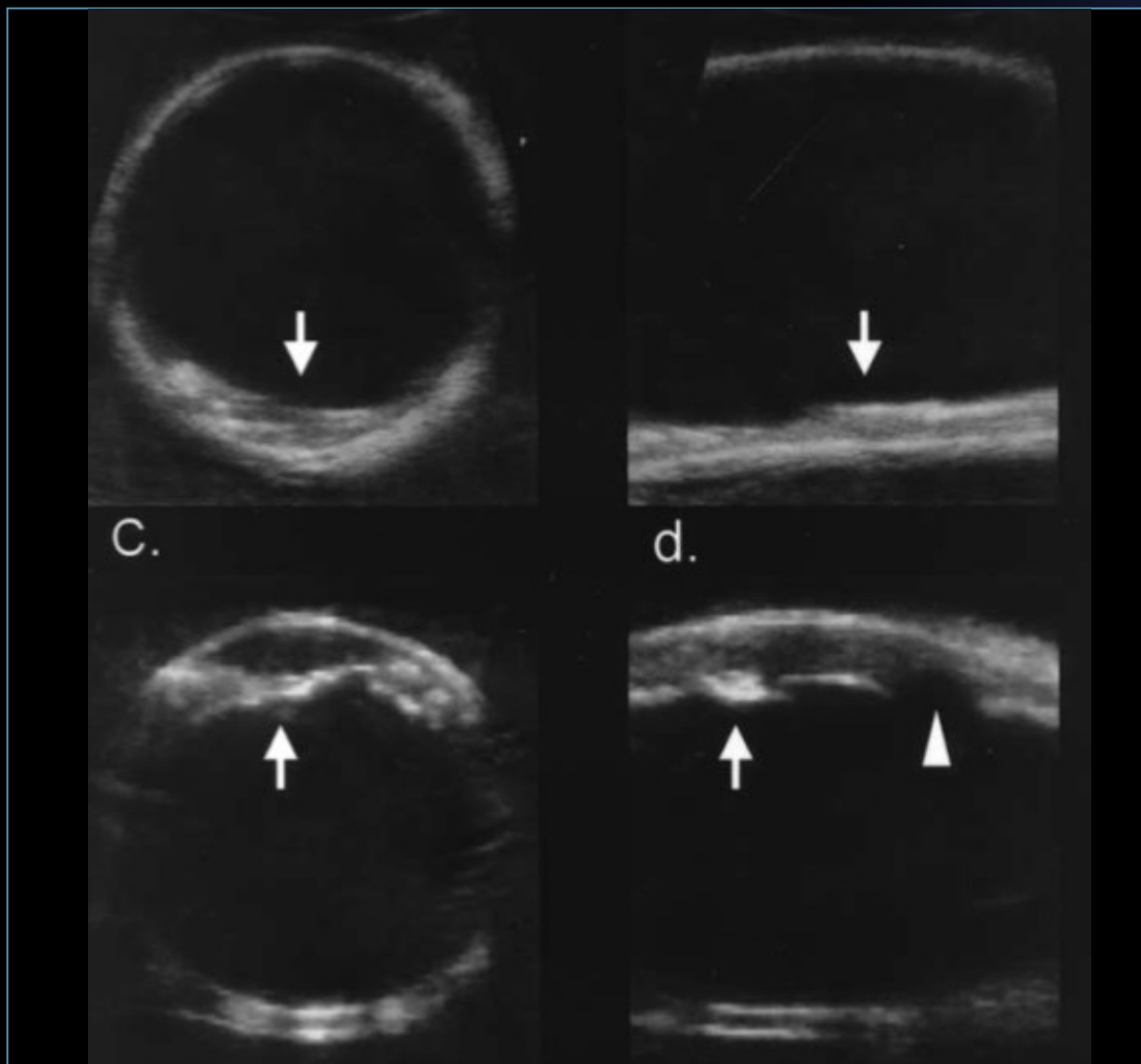
- Role of off pump CABG
- Management of atrial fibrillation/anticoagulation
- Role of preoperative screening for carotid disease
- Role of dual anti-platelet therapy (DAPT)
- Role of statins



**CME** **Guidelines for the Performance of a Comprehensive Intraoperative Epiaortic Ultrasonographic Examination: Recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists; Endorsed by the Society of Thoracic Surgeons**



# Ascending Aortic Atherosclerosis



# Timing of Stroke



	CABG	PCI
<b>Total</b>	<b>25 (2.8%)</b>	<b>12 (1.4%)</b>
Pre-procedure	3 (0.3%)	0
Procedural- 30 days	9 (1%)	2 (0.2%)
30 days- 1 Year	7 (0.8%)	3 (0.3%)
1- 2 years	6 (0.6%)	7 (0.7%)

# Message/ Lessons for Surgeons



- Screen the ascending aorta on all patients
- Perform an off pump “no touch” aortic technique if disease present
- Aggressive treatment of post operative AF +/- anticoagulation
- Determine if any benefit to DAPT after CABG
- Don't wait so long between randomization and treatment when you participate in RCT's