

# **Preoperative Cardiac Stents**

## **Perioperative Management**

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# Revasc prior to NCS

- If it offered long term benefit--made sense to do it
- 1-2 vessel CAD by angiogram, no benefit to revasc compared with aggressive med management
- PCI with DES increase risk if antiplatelet is interrupted for NCS?

# Stent Therapy

- Number of PCI > CABG
- Stents used in majority of PCIs
  - Increase procedural success
  - Decrease restenosis rates
- BMS vs. DES
  - Prevents restenosis
  - March 2003-Sirolimus-eluting (Cypher®)
  - April 2004-Paclitaxel-eluting (Taxus®)
  - 2005, 85% of stents were DES

# Stent Thrombosis

## ➤ Risks

- Suboptimal angiographic result
- High risk lesions
  - Small
  - Bifurcated lesions
  - Overlapping DES
- Diabetes
- Renal failure
- Low EF

## ➤ Prevention

- Good Angiographic results
- Dual antiplatelet therapy
- Regional vs. GA
  - 1993 study of arterial thrombosis (Rosenfield et al. Anesthesiology)

# Stent Thrombosis DES

- Risk between 0.5%-3.5%
  - Catastrophic outcomes
  - Fatality rate 45%-75%
  - MI rates 25%-65%
- 
- Degree of endothelial coverage
  - Intensity of antiplatelet therapy

Newsome, LT, et al. Coronary Artery Stents: Part I. Evolution of Percutaneous Coronary Intervention. *Anes & Anal* 2008;107 (2):552-569.

# Stent evaluations

## ➤ BMS

- Complete endothelialization by 28 days

## ➤ DES

- Incomplete healing, fibrin deposition and inflammatory cells at 6 months

## ➤ Sirolimus activates platelets and induces aggregation

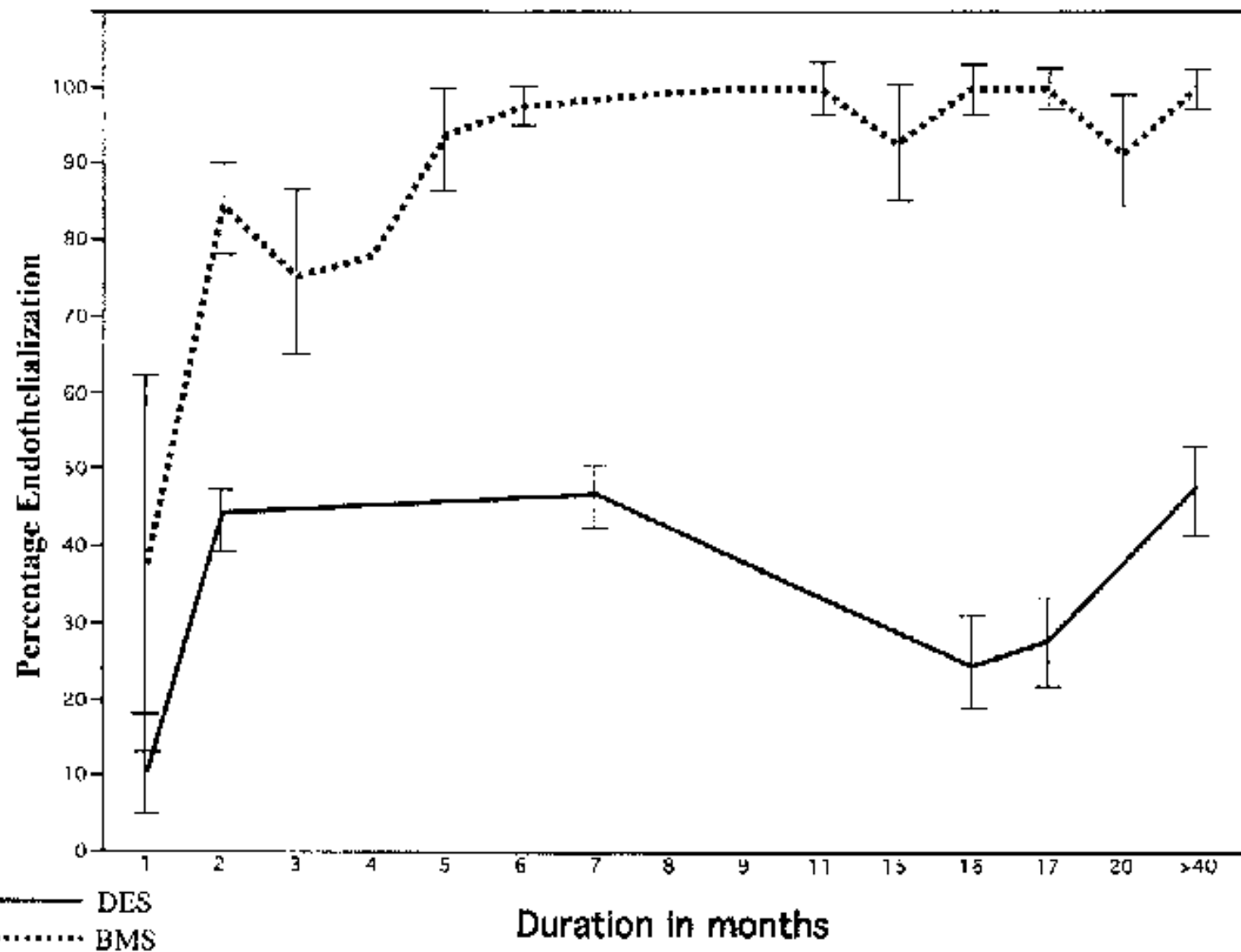


Fig. 5. Endothelialization of DES and BMS. The percentage of endothelialization was significantly higher in the BMS group than in the DES group at all time points (p < 0.05).

# Premature Discontinuation

- Greatest Predictor of stent thrombosis
- Premier Registry
  - 500 patients with acute MI with DES
  - 7.5% mortality rate among patients who prematurely d/ced thienopyridine treatment
  - Pts who remained on ASA and clopidogrel had a 0.7% mortality rate

Spertus et al. Prevalence, predictors and outcomes of premature discontinuation of Thienopyridine therapy after drug-eluting stent placement: results from the PREMIER Registry. *Circulation* 2006;113:2803-9.



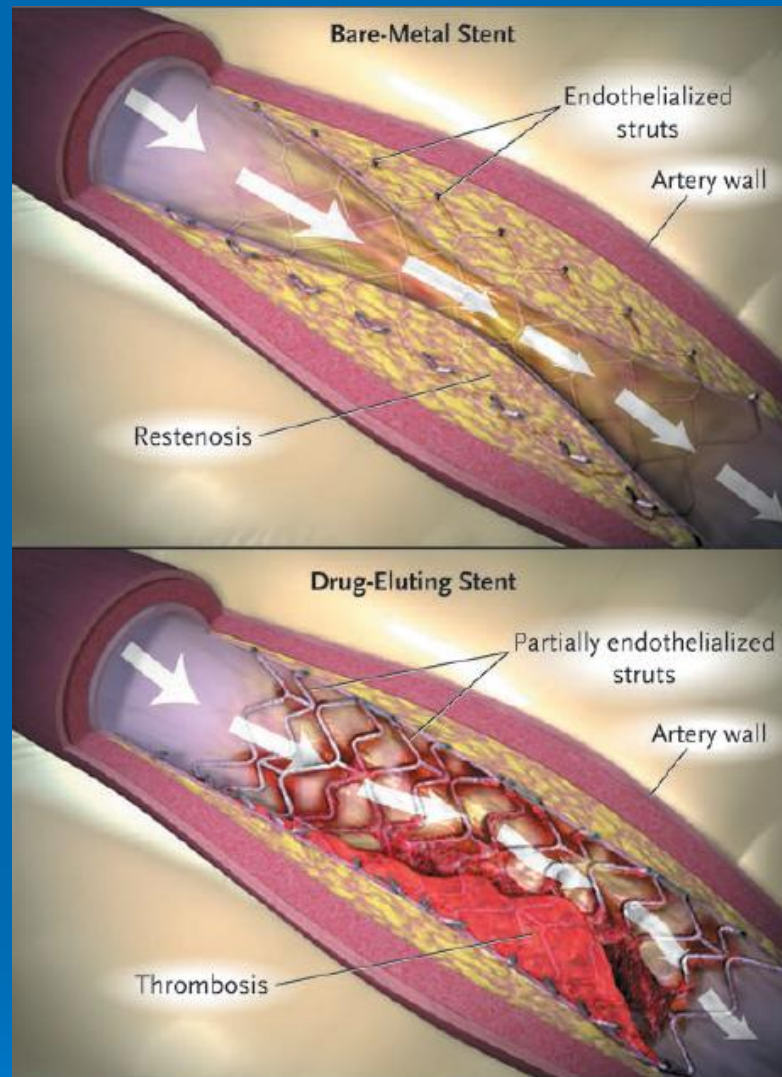
# Catastrophic Outcomes

- Kaluza in 2000 NCS within 6 wks of PCI
- NCS after PCI--40 patients with BMS
  - 7 MI
  - 11 major bleeds
  - 8 deaths
- Posner
  - PCI within 90 days of NCS associated with complication rates similar to patients with CAD without revasc

# BASKET LATE

- How long to treat with antiplatelet agents to prevent late events
- What happens after antiplatelet therapy ends

neointimal  
hyperplasia



thrombus

**Figure 1. Potential Complications of Coronary Stenting: Restenosis in a Traditional Bare-Metal Stent and Late Thrombosis in a Drug-Eluting Stent.** Arrows indicate blood flow. An animation showing restenosis and stent thrombosis can be viewed at [www.nejm.org](http://www.nejm.org).

# BASKET LATE

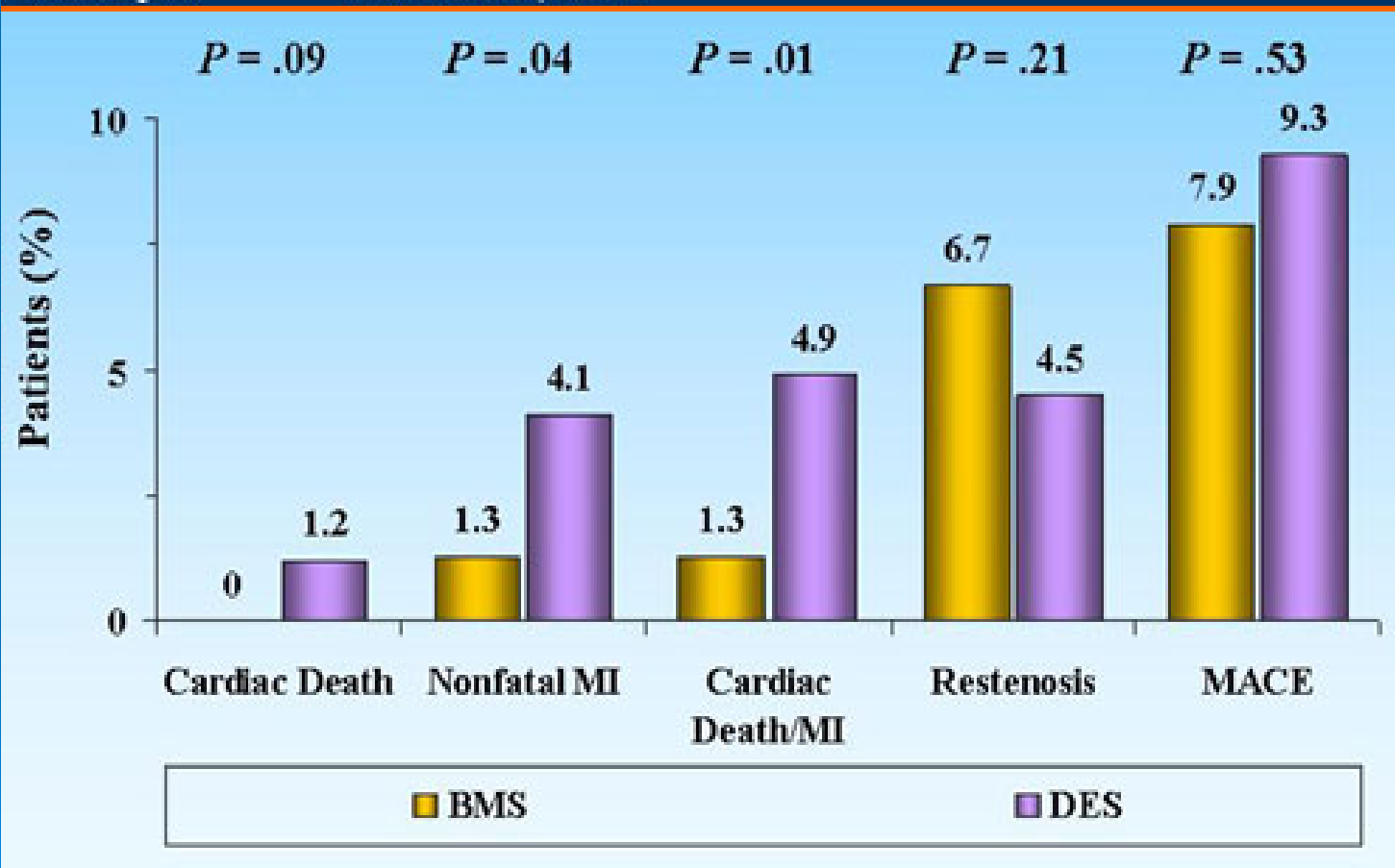
- RCT DES vs BMS (2:1 ratio)
- Survived 6 months without event
- Stopped clopidogrel
- Followed for an additional 12 months
- Late clinical events (7-18 mth)
- Late stent thrombosis (7-18 mth)

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit Benefit of Drug Eluting Stents. JACC 2006 48:12;2584-91.

# BASKET LATE

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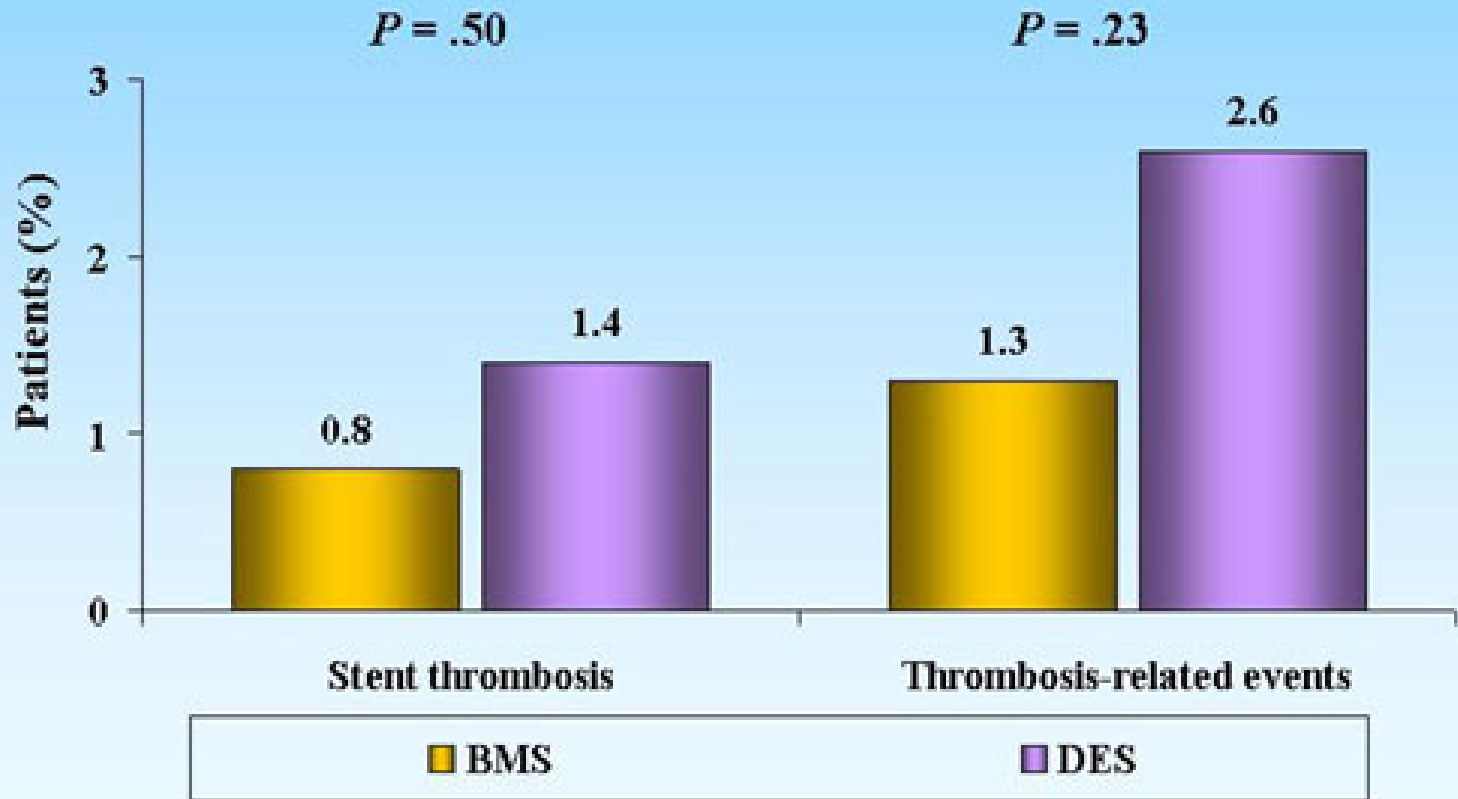
Nonfatal MI and cardiac death/MI were higher

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit

# BASKET LATE

Medscape®

www.medscape.com



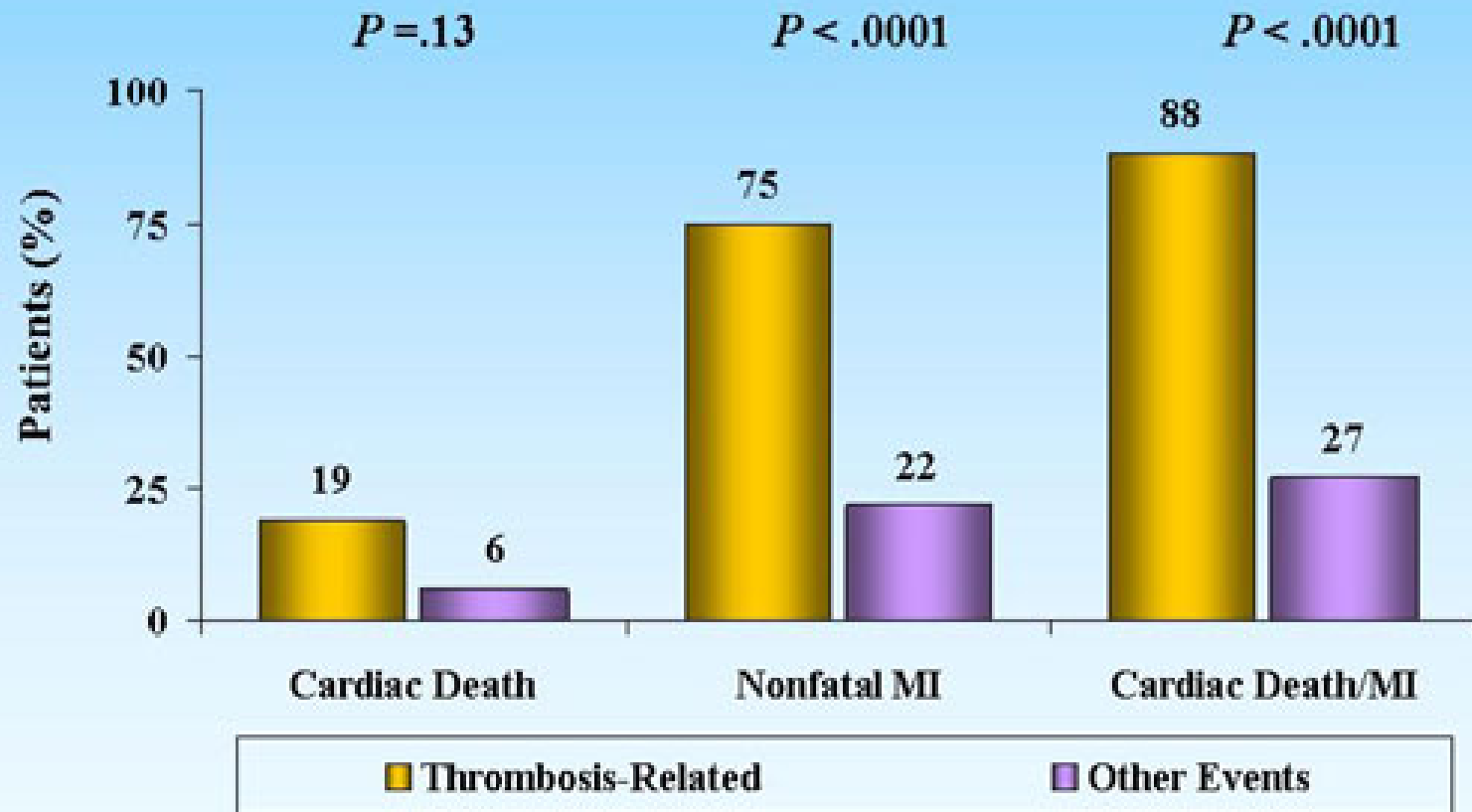
Angiographic thrombosis rates the same

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit

# BASKET LATE

Medscape®

www.medscape.com



Thrombosis related event much higher risk of bad outcome  
Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit

# BASKET LATE

- Thrombosis related event
  - Median time 116 days
  - Range between 15 days to 362 days

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit Benefit of Drug Eluting Stents. JACC 2006 48:12;2584-91.



# BASKET LATE

- Benefit of lower rate of reinterventions vs. late complication
- Late stent thrombosis after discontinuation of clopidogrel may limit net clinical benefit

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit Benefit of Drug Eluting Stents. JACC 2006 48:12;2584-91.

# BASKET LATE

- Conclusions--Clopidogrel discontinuation
  - Late stent thrombosis
    - 2-3 times higher in patients with DES
    - Carried 4 times higher risk of cardiac death or MI vs non thrombosis related events
    - Occurred after 1 year after drug termination
    - More frequent in following patients
      - Previous MI
      - Need for IIb/IIIa inhibitors initially
      - DES

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit Benefit of Drug Eluting Stents. JACC 2006 48:12;2584-91.

# BASKET + BASKET LATE

- In 100 patients
  - May avoid 5 major cardiac events/interventions at 6 months but lead to 3 patients suffering cardiac death or nonfatal MI during months 7-18

Pfisterer, M. et al. Late Clinical Events After Clopidogrel Discontinuation May Limit Benefit of Drug Eluting Stents. *JACC* 2006 48:12;2584-91.

# Camenzind et al 09/06

- Meta-analysis of all company supported RCT--3 yr follow up
- Sirolimus-DES 60% relative increase in death or MI (P = 0.03)
- Paclitaxel- DES 15% increase (NS)
- “late stent thrombosis and discontinuation of antiplatelet therapy caused higher rates of death and MI

# FIRESTORM 2007-2008

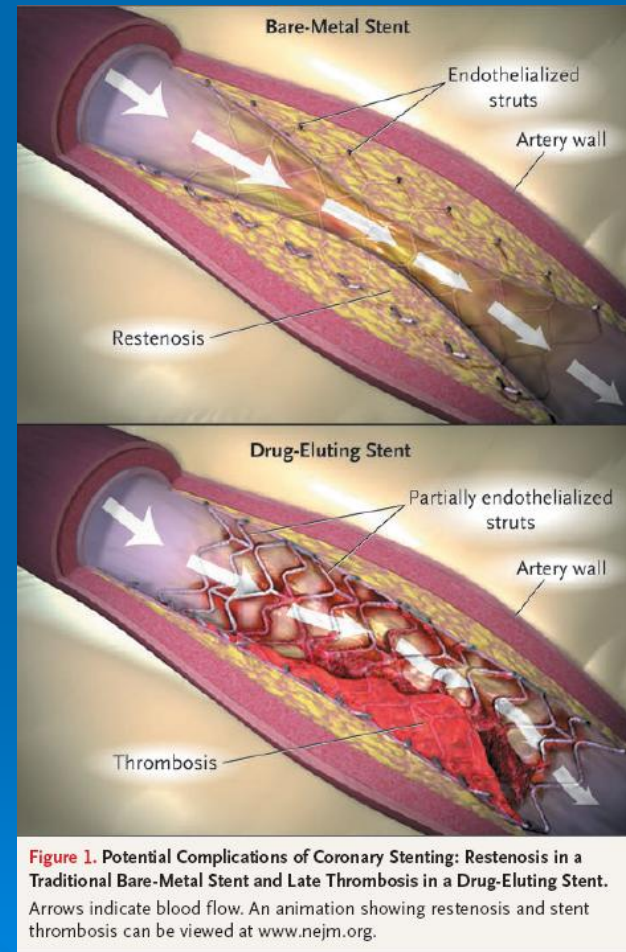
- Redefined definitions of stent thrombosis
- Reanalysis of data sets
  - Mauri NEJM 2007--no difference yet small study
  - Stone NEJM 2007--small yet significant increase with DES over 1-4 yrs
  - Spaulding NEJM 2007--increase in death and MI with DES, better outcomes with BMS in diabetics

# ACC/AHA Recommendations

- ASA 325 mg non enteric indefinitely
- Minimum 3 months clopidogrel for sirolimus-coated (Cypher®) stents
- Minimum 6 months clopidogrel for paclitaxel-coated (Taxus®) stents
- 12 months clopidogrel optimum
- 12 months minimum?

# DES vs. BMS

- Impair healing
- Lower in stent stenosis
- Delay endothelialization
- “thrombogenic surface”
- Low risk vs high risk lesions
- Accelerated periop



# Clopidogrel and DES

## Long term outcome

- Landmark analysis technique
  - 6 month clopidogrel use (yes or no)
  - 12 month clopidogrel use (yes or no)
  - 4666 patients
    - 3165 with BMS
    - 1501 with DES

Eisenstein, EL, et.al. Clopidogrel Use and Long-term Clinical Outcomes After Drug-Eluting Stent Implantation. JAMA 2007;297:159-168.



# Clopidogrel and DES

## Long term outcome

- Patients with long term clopidogrel with DES significantly improved prognosis
  - Significantly lower death and death or MI compared with patients with DES not receiving the medication
- Continued clopidogrel therapy conveys important prognostic benefit for patients with DES although not seen for BMS

Eisenstein, EL, et.al. Clopidogrel Use and Long-term Clinical Outcomes After Drug-Eluting Stent Implantation. *JAMA* 2007;297:159-168.

# Perioperative

- Hypercoagulable
  - Platelet activation
  - Reduced Fibrinolytic activity
  - Procoagulant clotting factors increase
- Inflammatory
- Hemodynamic changes
- Platelet transfusions?

# NCS and Cardiac Stenting

- Retrospective review-PCI up to 2 yr prior to NCS
  - Surgical procedure
  - 30 day CV outcome
  - No periop antiplatelet therapy protocol
    - Some received through procedure
    - Some stopped 1 week prior to OR

Schouten, O, et al. Noncardiac Surgery after Coronary Stenting: Early Surgery and Interruption of Antiplatelet Therapy are Associated with an Increase in Major Adverse Events. *JACC* 2007 49:1;122-125.

# NCS and Cardiac Stenting

- 30 day MACE
  - Nonfatal MI
  - Cardiac death
- 192 patients surgery within 2 yrs
  - Early surgery (clopidogrel required 1/3/6 mths from trial studies)
  - Late surgery

Schouten, O, et al. Noncardiac Surgery after Coronary Stenting: Early Surgery and Interruption of Antiplatelet Therapy are Associated with an Increase in Major Adverse Events. JACC 2007 49:1;122-125.

# NCS and Cardiac Stenting

- First 30 days-5 MACE all fatal
  - Early surgery group 4 MACE (13.3%)
  - All these patients discontinued their antiplatelet agents (31%)
  - No MACE in patients who continued therapy
  - Late surgery group 1 MACE (0.6%)
- No difference in blood transfusion in those who discontinued antiplt therapy

Schouten, O, et al. Noncardiac Surgery after Coronary Stenting: Early Surgery and Interruption of Antiplatelet Therapy are Associated with an Increase in Major Adverse Events. JACC 2007 49:1;122-125.

# NCS and Cardiac Stenting

## Conclusions

- “Association between early NCS after Cardiac stenting and perioperative adverse cardiovascular events”
- “discontinuation of antiplatelet therapy during the perioperative period may be a major cause of the increase in MACE.”
- “antiplatelet therapy throughout”

# AHA/ACC/SCAI/ACS/ADA

- Prevention of Premature Discontinuation of Dual Antiplatelet Therapy in Patients with Coronary Artery Stents
  - 12 months of dual therapy
  - Education
  - Collaboration

Grines, CL, et al. AHA/ACC/SCAI/ACS/ADA Science Advisory, Prevention of Premature Antiplatelet Therapy in Patients with Coronary Artery Stents. *Circulation* 2007;115:813-818

# AHA/ACC/SCAI/ACS/ADA

- Premature discontinuation-non surgical patients
  - Catastrophic stent thrombosis
  - Occurs between 8%-30% of patients
  - Pooled analysis 6 trials
    - Incidence of MI or death 64.4%
  - “doubling the rates of MI and death”

Grines, CL, et al. AHA/ACC/SCAI/ACS/ADA Science Advisory, Prevention of Premature Antiplatelet Therapy in Patients with Coronary Artery Stents. *Circulation* 2007;115:813-818



# AHA/ACC/SCAI/ACS/ADA

- Surgical patients
- Kaluza 2000 40 patients
  - 7 MI, 6 fatal, 5 off meds
- Sharma 2004 47 patients
  - 6 of 7 deaths in manner c/w stent thrombosis
- Patients infarct in OR or PACU

Grines, CL, et al. AHA/ACC/SCAI/ACS/ADA Science Advisory, Prevention of Premature Antiplatelet Therapy in Patients with Coronary Artery Stents. *Circulation* 2007;115:813-818

# AHA/ACC/SCAI/ACS/ADA

- Stent thrombosis 29% of patients who discontinue antiplatelet therapy early
- Mortality rate for stent thrombosis is 20-45%
- Early discontinuation of antiplatelet is greatest predictor

# AHA/ACC/SCAI/ACS/ADA

## ➤ Factors to discontinue drugs

- Patients
  - Cost
  - Education
  - Elderly
  - Lack of follow-up/cardiac rehab
- Health care providers
  - Misguided concerns about bleeding
  - Lump all anticoags together

# AHA/ACC/SCAI/ACS/ADA Recommendations

- Educate and avoid in non compliant patients
- Avoid if surgical procedure planned within next 12 months
- Education prior to discharge importance and significance of early discontinuation
- Contact cardiologist if going to stop or instructed to stop by other health care provider

# AHA/ACC/SCAI/ACS/ADA

- Proceduralist must know risk, communicate with cardiologist
- Delay elective procedures--12 months DES, 1 month minimum for BMS
- DES and procedures and d/c clopidogrel, continue ASA and restart clopidogrel ASAP

# Clopidogrel Forever

- Everyone with DES?
- Acute coronary syndrome
- Long stents
- Multiple stents
- Overlapping stents
- Diabetes
- Renal failure

# Newsome Perspective

## Wake Forest

- No elective surgery
  - 12 months DES
  - 3 months BMS
- Urgent procedure and anyone on team wants to stop antiplatelet therapy-- patient's cardiology consult
- Never stop ASA-if held, resume and wait 2 hours before OR

# Bridging Therapy

- Integrillin--GP IIb/IIIa inhibitor
  - Prevent activation and aggregation
- Heparin
  - Prevent thrombin formation
- IV therapy
- Hold 6 hours preop

Newsome, LT, et al. A Protocol for the Perioperative Management of Patients With Intracoronary Drug-Eluting Stents. APSF; Winter Newsletter 2007.



# Bridging Therapy

- Only if clopidogrel must stop
- Cardiologist documents
  - Type of DES placed and date
  - Coronary complexities
  - Comorbidities (CRF, DM, low EF)
- Clopidogrel held 5 days preop (cardiologist must approve)

# Bridging Therapy

- ASA throughout
- Admit patient 2 days preop to surgical service
- Start Bridge therapy

|                       |                    |                   |
|-----------------------|--------------------|-------------------|
| Normal renal function | 180 mcg/kg IV load | 2.0 mcg/kg/min CI |
| Cr > 2.0, Clcr < 50   | 180 mcg/kg IV load | 1.0 mcg/kg/min CI |

IV Heparin to keep PTT 70-90

# Bridging Therapy

- Hold infusions 6 hour preop
  - Cardiology and surgery
    - Resume clopidogrel or integrillin ASAP (post op night)
    - Clopidogrel load 600 mg p.o.
    - Clopidogrel maintainance 75 mg p.o. daily
- or
- Integrellin protocol

Newsome, LT, et al. A Protocol for the Perioperative Management of Patients With Intracoronary Drug-Eluting Stents. APSF; Winter Newsletter 2007.

# Bridging Therapy

- Small studies/reports
- Not tested
- Not accepted as standard

# Perioperative Management of Patients with Coronary Stents

## ➤ Prevention

- Avoid preop revascularization
- Revascularize without stents
- Appropriate stent selection
- Delay surgery after stent placement
- Continue antiplatelet therapy
- Improve awareness of all MDs caring for these patients

# Avoid Revascularization Preop

- **Corn Art Revasc Prophylaxis (CARP)**
  - 510 patients undergoing vascular surgery
    - 33% AAA, 67% lower extremity revasc
    - Excluded LM disease, unstable angina, CM
    - 41% CABG vs 59% PCI
  - **Revasc vs No revasc preop**
    - No difference in postop AMI (8.4% both groups)
    - Median survival 27 months (78%)

McFalls EO, et al. Coronary-artery revascularization before elective major vascular Surgery. NEJM 2004;351:2795-2804.

# Revasc without stent

- 350 patients NCS within 2 mths of balloon only PCI
  - 1 death, 2 Mis
- Acceptable results
- May be alternative if surgery is needed (within 4 to 6 weeks)
- Gray zone
  - To early risk for sub acute or acute thrombosis
  - To late risk for restenosis

# Stent Selection Preoperatively

- Surgery needed within 12 mths
  - BMS
- Surgery can wait
  - DES--1 year vs. forever at risk?
  - If DES is needed
    - Prefer sirolimus stent (CYPHER) 3 mth rule



# Delay Surgery

- BMS
  - 4 to 6 week minimum
- DES
  - 12 month minimum

# Continue Antiplatelet Therapy

- Optimal length of dual antiplatelet treatment unknown
- Continue both agents--risk of bleeding

- Safe

- Dental extractions
- Cataract surgery
- Routine dermatologic surgery

- Higher bleeding risk

- Risk of thrombosis,MI and death > bleeding

- Unsafe

Neurosurgery

# Stop and Bridge

- Does not offer complete protection
  - Must be continued into the post op period as this is the greatest risk period
  - Expensive
  - Logistically difficult
  - Unproven

# Stop and Go

- Only used when absolutely necessary secondary to bleeding risk
  - Neurosurgical cases
- Reload with 600 mg
  - Takes effect within 2-4 hours
  - Prevents hyporesponsiveness

# Education

## ➤ Anesthesiologist survey

63% unaware of current recommendations

33% recommended no delay, or a delay of 1-2 weeks following “stent” placement

Patterson L. et.al. Appropriate waiting time for noncardiac surgery following coronary Stent insertion: views of Canadian anesthesiologist. Can J Anaesth 2005;52:440-441

# Preoperative Planning

- Stent type (BMS, SES, PES)
- Stent location
- Date of implantation
- Consult interventional as well as patient's cardiologist

Brilakis, ES, etal. Perioperative Management of Patients with Coronary Stents.  
JACC, 2007;49:2145-2150.

# Preoperative Planning

- Joint decision with input from anesthesia, cardiologist and surgeon
  - Timing of surgery
  - Appropriate antiplatelet management
- Perform surgery in centers with 24 hour interventional cardiology coverage available to treat stent thrombosis with immediate PCI

# Stent Thrombosis Treatment

- ST elevation acute MI
- Treatment early reperfusion
  - Thrombolytics contraindicated
  - Primary PCI treatment of choice
    - ASA
    - Single dose of heparin or bivalirudin



# Stent Thrombosis Treatment Outcomes

- Retrospective analysis 2001
  - 48 patients with MI within 1 week of NCS
    - Heparin and ASA
    - 65% survival with “early invasive strategy”
    - High frequency of cardiogenic shock and arrest
    - 1 patient with significant operative site bleeding (TKA)
    - Included intrathoracic and neurosurgical cases

Berger, PB.etal. An Immediate Invasive Strategy for the Treatment of Acute Myocardial Infarction Early after NCS. Am J Cardiol 2001;87:1100-1102.

# Real World

- Patient in ASC-outpatient surgery
- Off both agents because “told to stop”
- Now what
  - ASA--325 mg
  - Cancel case reschedule in 3-5 days to allow ASA to work and get more information
  - Do later in day after 2-4 hours
  - If surgeon wants to proceed, must know rates of stent thrombosis and mortality

# Real World

- Avoid platelet transfusion unless absolutely necessary
  - Increase activity and aggregation without increase count
  - Sympathetic activation and cytokines
  - Enhances prothrombotic state