PCI in the Era of Drug-Eluting Stents

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INTRODUCTION

Coronary stenting is the most frequently performed PCI representing over 80% of the intervention done world wide .

Compared to balloon angioplasty , coronary stenting has more favorable outcome and its angiographic restenosis rate is only 10% to 20% in short lesions and large vessels.

ISR,however, in over 30% to 60% of patients with high risk group like diabetes, small vessels, long segment lesions.

A Brief History of Stenting

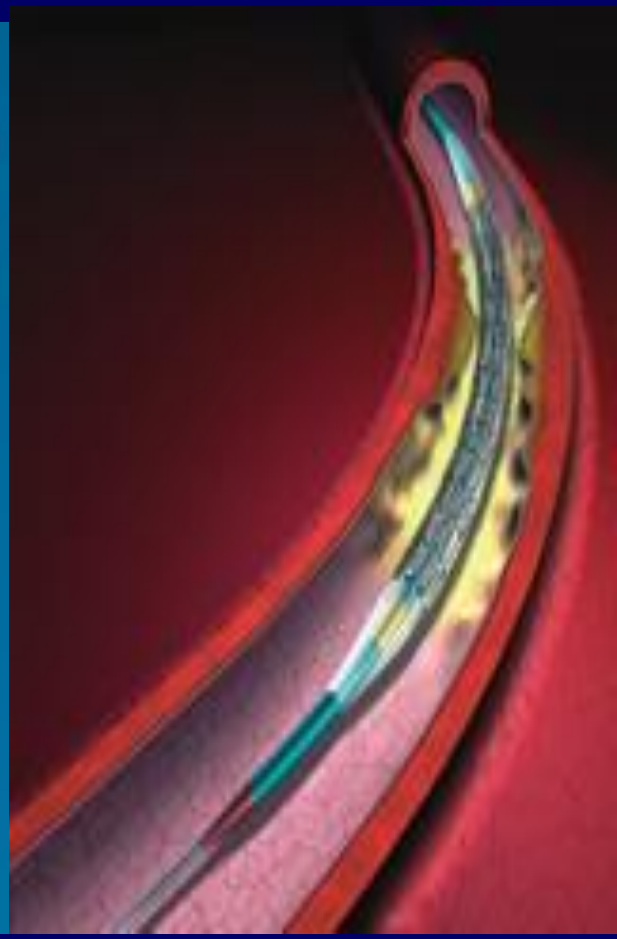
Concept of the Stent grew with plain balloons angioplasty in the first decade of its use.

Wall of the coronary artery weakened after balloon dilatation.

In some cases, the artery would collapse after the balloon was deflated.

The only option was emergency bypass graft surgery to repair the problem.

CORONARY STENT



The First Stents

In 1986 in Toulouse, France, the first stent inserted into a human coronary artery.

Simultaneous development in US and Europe.

Several generations of bare metal stents were developed, with each succeeding other being to overcome the limitations of previous one.

A Persistent Problem

Restenosis persisted typically at six-months in about 20-30% and in some cases more than that.

Although the rates were low compare to POBA.

Restenosis is not a recurrence of coronary artery disease.

It is the body's response to "controlled injury" of angioplasty

Growth of smooth muscle cells analogous to a scar.

Restenosis

- Mechanism of Restenosis
  - Arterial Injury
  - Immune Response
  - SMC Proliferation
  - Migration of SMCs
  - Initmal Proliferation
  - Healing

SOLUTION

- **Different treatment strategies were tried to reduce the restenosis rate with repeat balloon angioplasty, rotational atherectomy, laser angioplasty, cutting balloon Angioplasty, or repeat stenting,currently brachytherapy, but the restenosis rate is still high in high risk group.**

- **Now we have got the magic bullet "DRUG ELUTING STENT" which has already proved their efficacy by reducing the ISR dramatically.**

Development of Coated and Drug-Eluting Stents

The solution moved toward pharmacologic advances.

Variety of drugs were tested known to interrupt the biological processes that caused restenosis.

Drug-Eluting Stent (DES) Basics

DES is a normal metal stent coated with a pharmacologic agent

It has been extremely successful in reducing restenosis from the 20-30% range to single digits.

Three major components to a DES:

- **Type of stent that carries the drug coating**
- **Method by which the drug is delivered by the coating to the arterial wall (polymeric or other)**
- **The drug itself**

DSA - HOW IT WORKS

Anti-thrombotic

- Reduce platelet adhesion and fibrin binding

Anti-inflammatory

- Inhibit the body's immune response to the stent

Anti-proliferative

Intercept cell growth signaling pathways

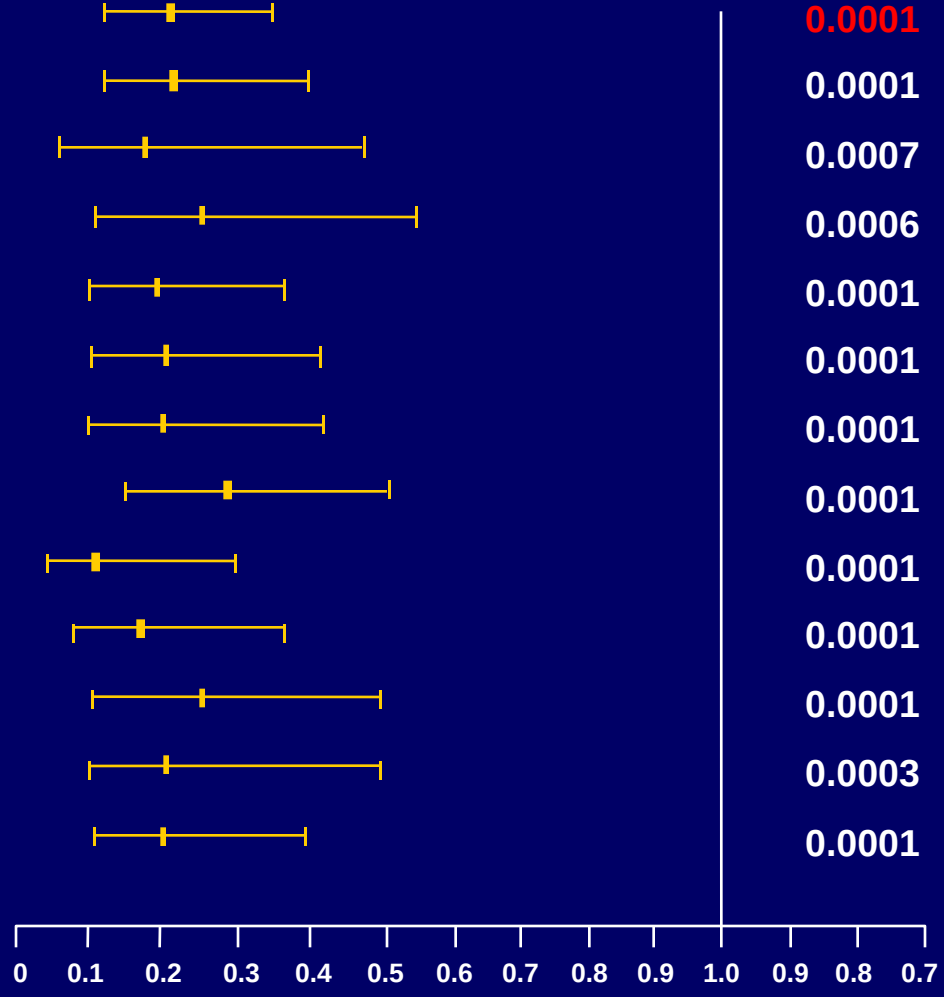
A promoter of healing

- Stimulate endothelial cell growth.

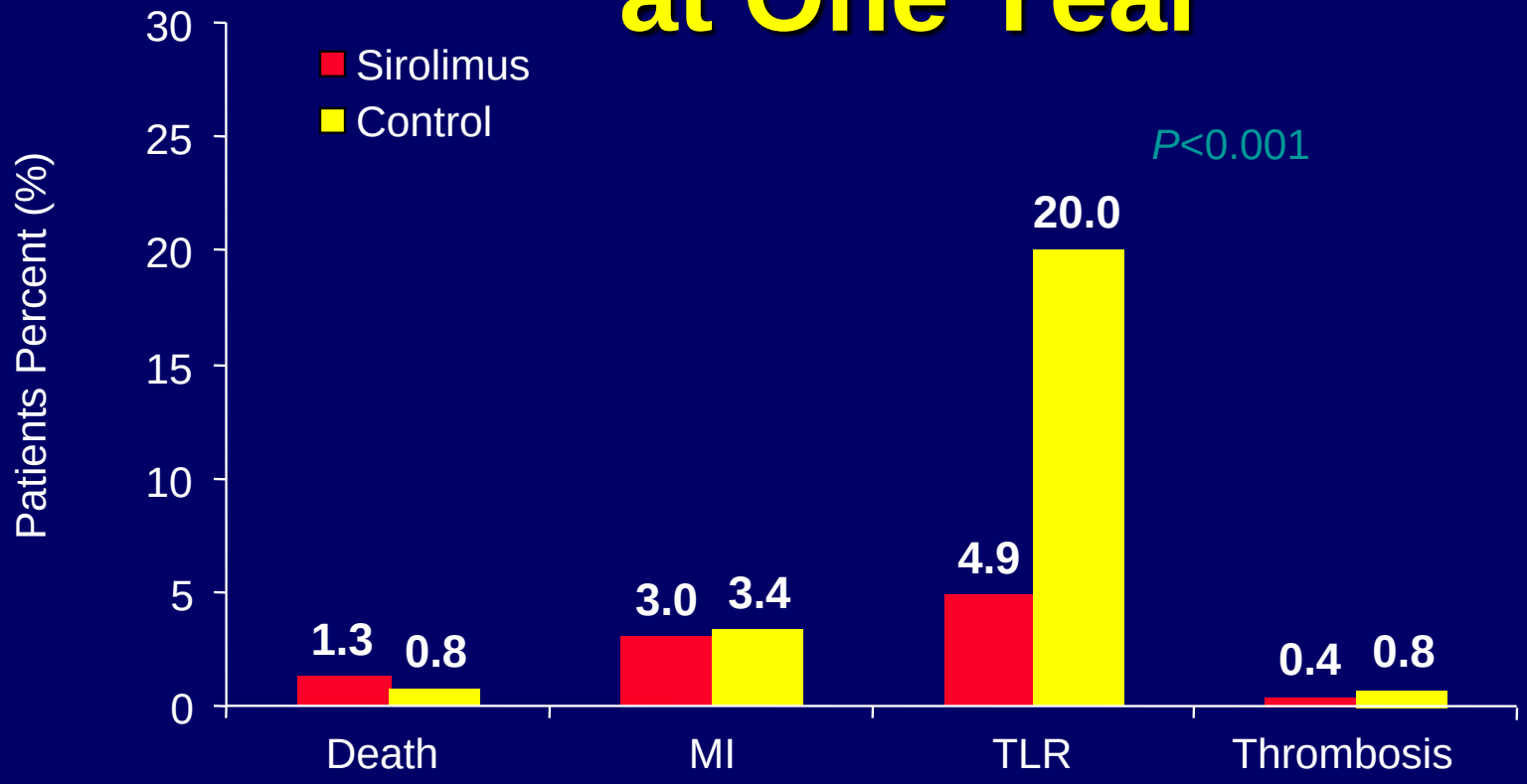
Harmless to normal cells

SIRIUS: TLR Events

	Sirolimus	Control	P-value	
Overall	4.1	16.6	0.0001	124
Male	4.4	16.6	0.0001	122
Female	3.4	16.5	0.0007	130
Diabetes	6.9	22.3	0.0006	154
No Diabetes	3.2	14.3	0.0001	111
LAD	5.1	19.8	0.0001	147
Non-LAD	3.4	14.3	0.0001	109
Small Vessel (<2.75)	6.3	18.7	0.0001	125
Large Vessel	1.9	14.8	0.0001	128
Short Lesion	3.2	16.1	0.0001	129
Long Lesion (>13.5)	5.2	17.4	0.0001	122
Overlap	4.5	17.7	0.0003	131
No Overlap	3.9	16.1	0.0001	121



SIRIUS: Clinical Events at One Year



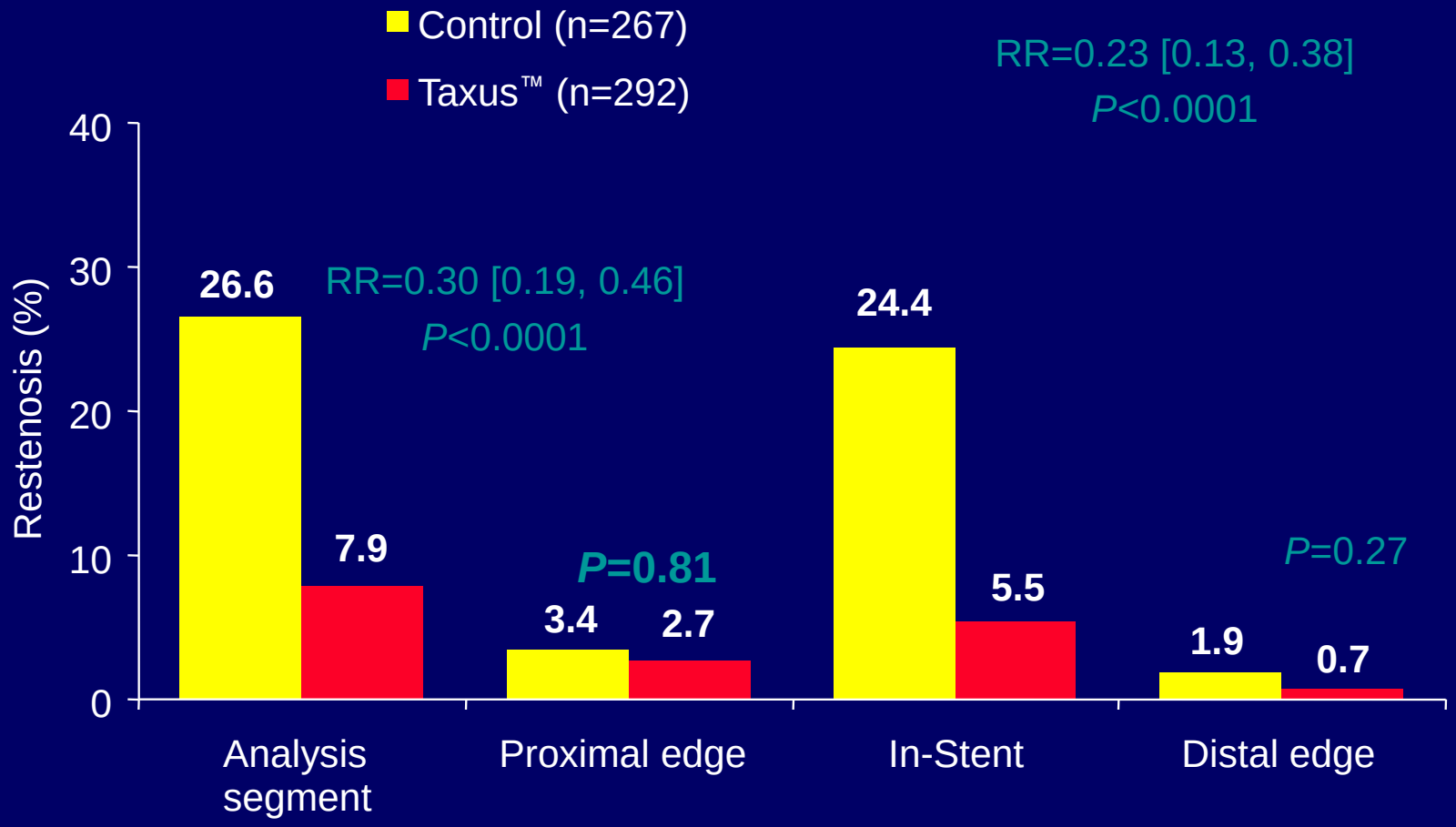
Clinical follow-up demonstrated effectiveness in reducing the incidence of repeat revascularization without any excess of adverse events
No effect on late MI or death compared to BMS

Holmes DR. *Circulation.* 2004;109:634-640.

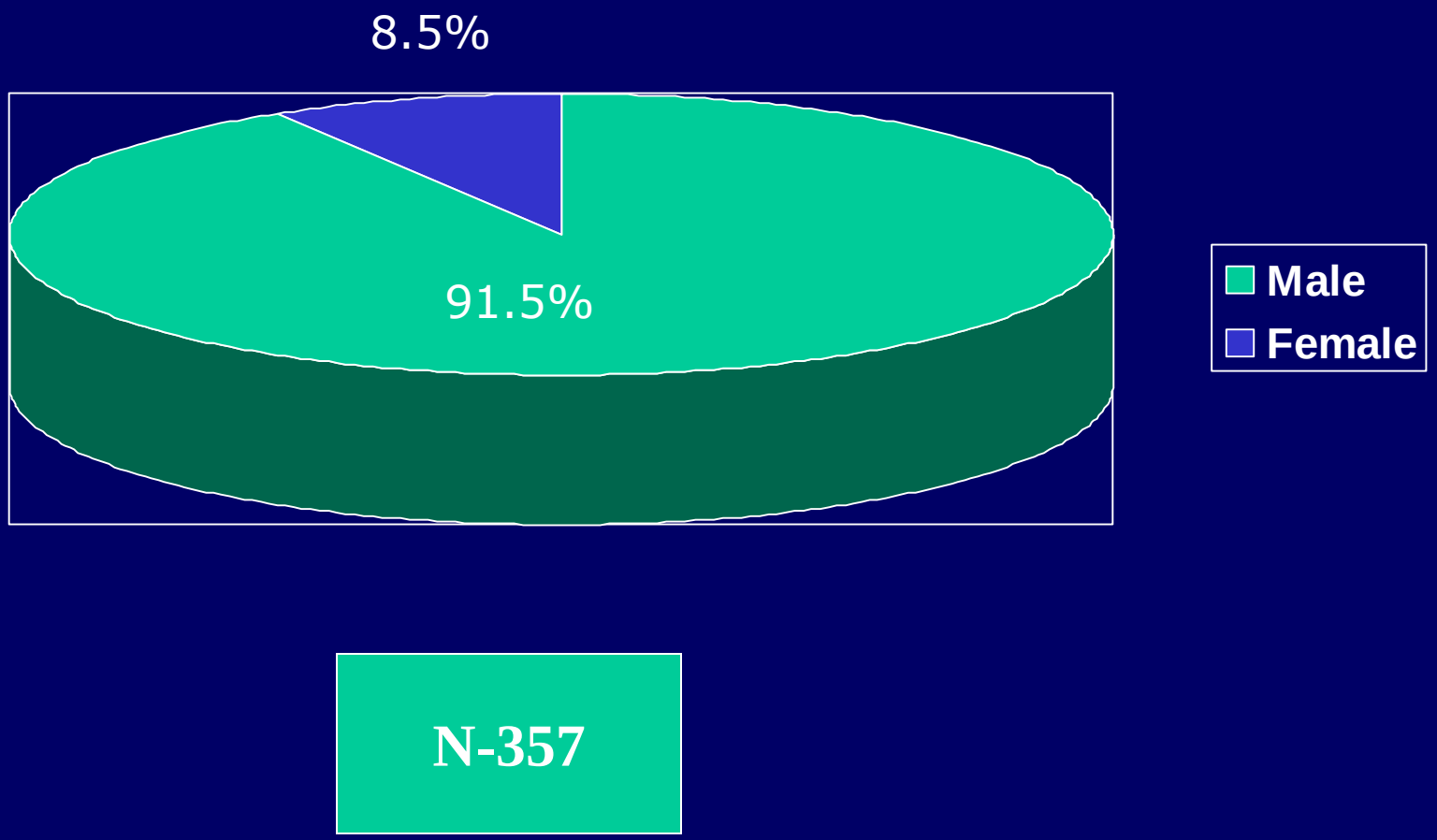
SIRIUS - Diabetic sub-group

	CYPHER n=131	Control n=148	P
Restenosis			
In-stent	**8.3**	**48.5**	**< 0.001**
In-segment	17.6	50.5	**< 0.001**
TLR (%)	6.9	22.3	**< 0.001**
MACE (%)	**9.2**	**25.0**	**< 0.001**

TAXUS 4
Restenosis Rate



Sex Distribution



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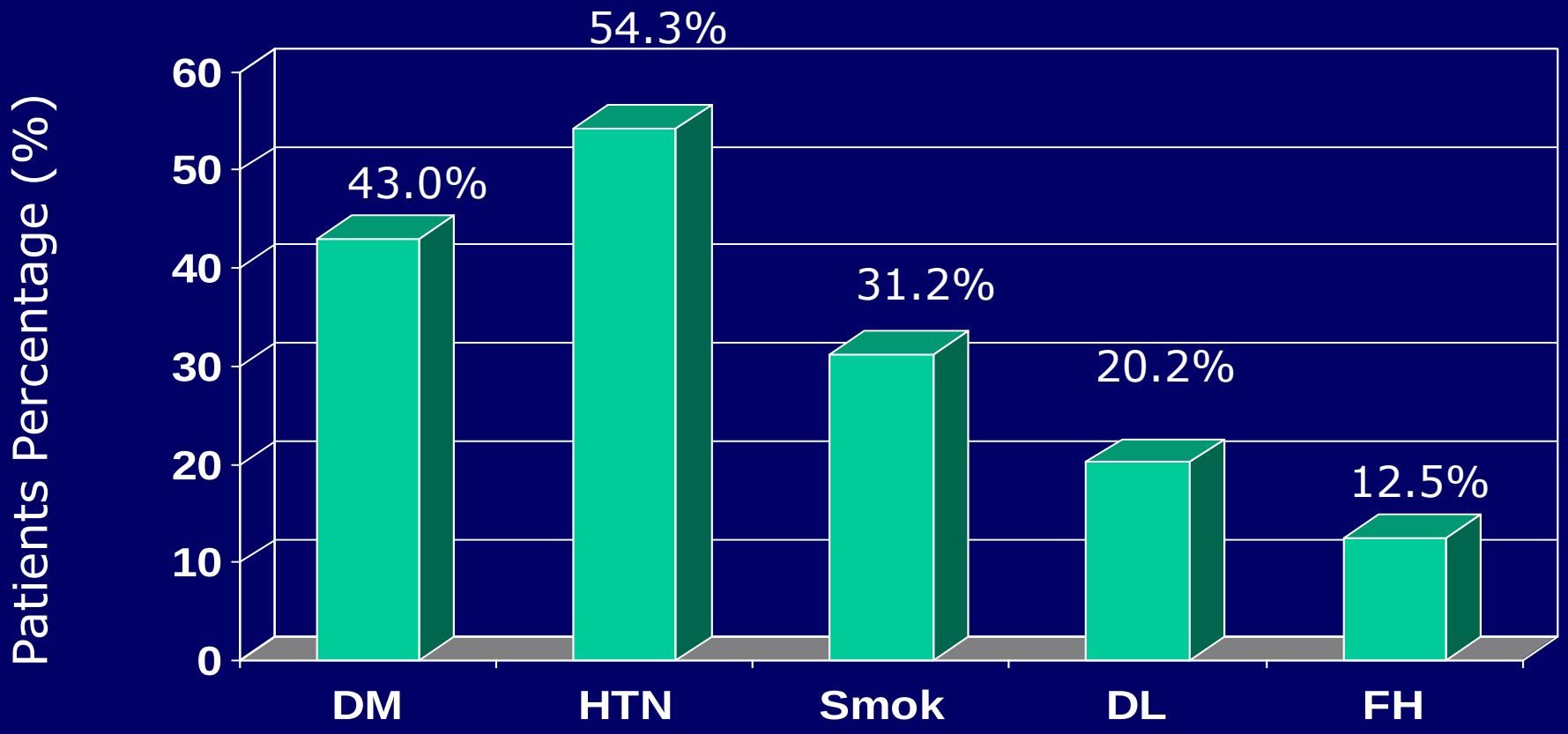
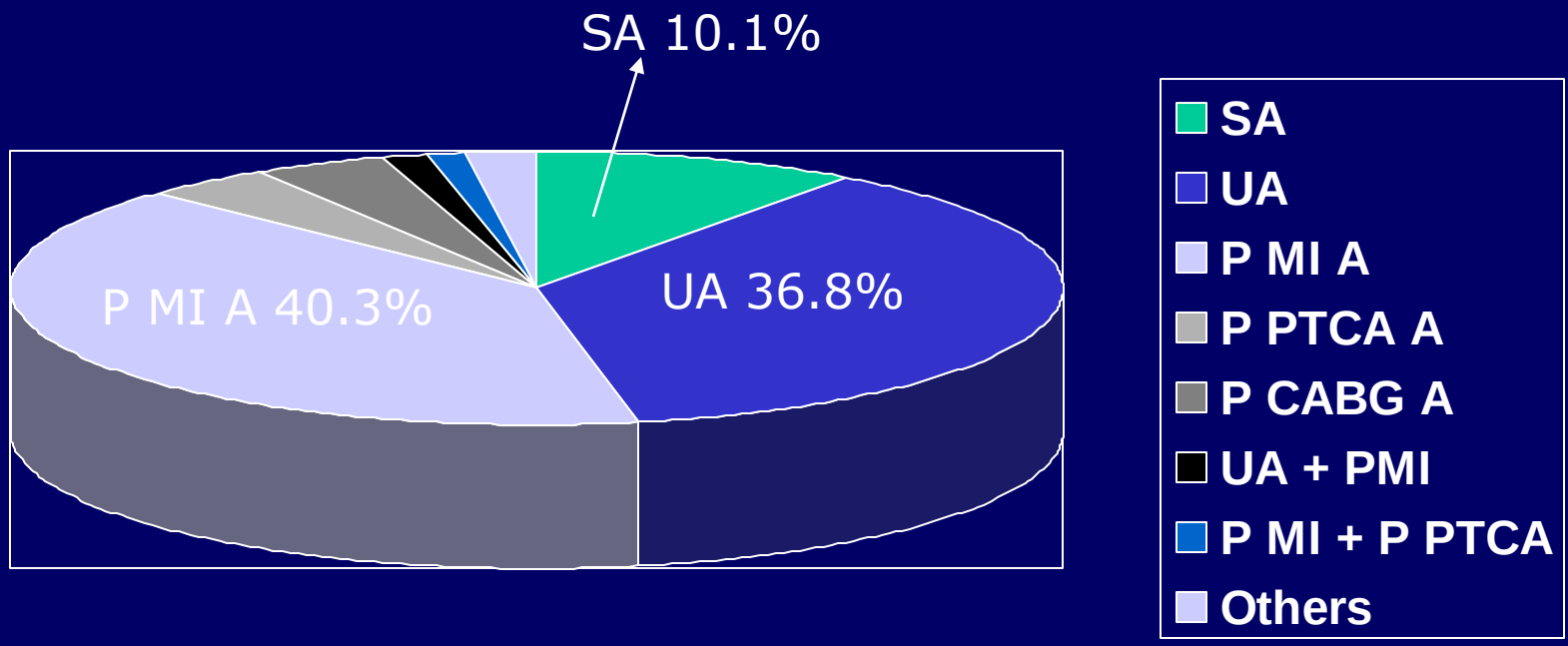
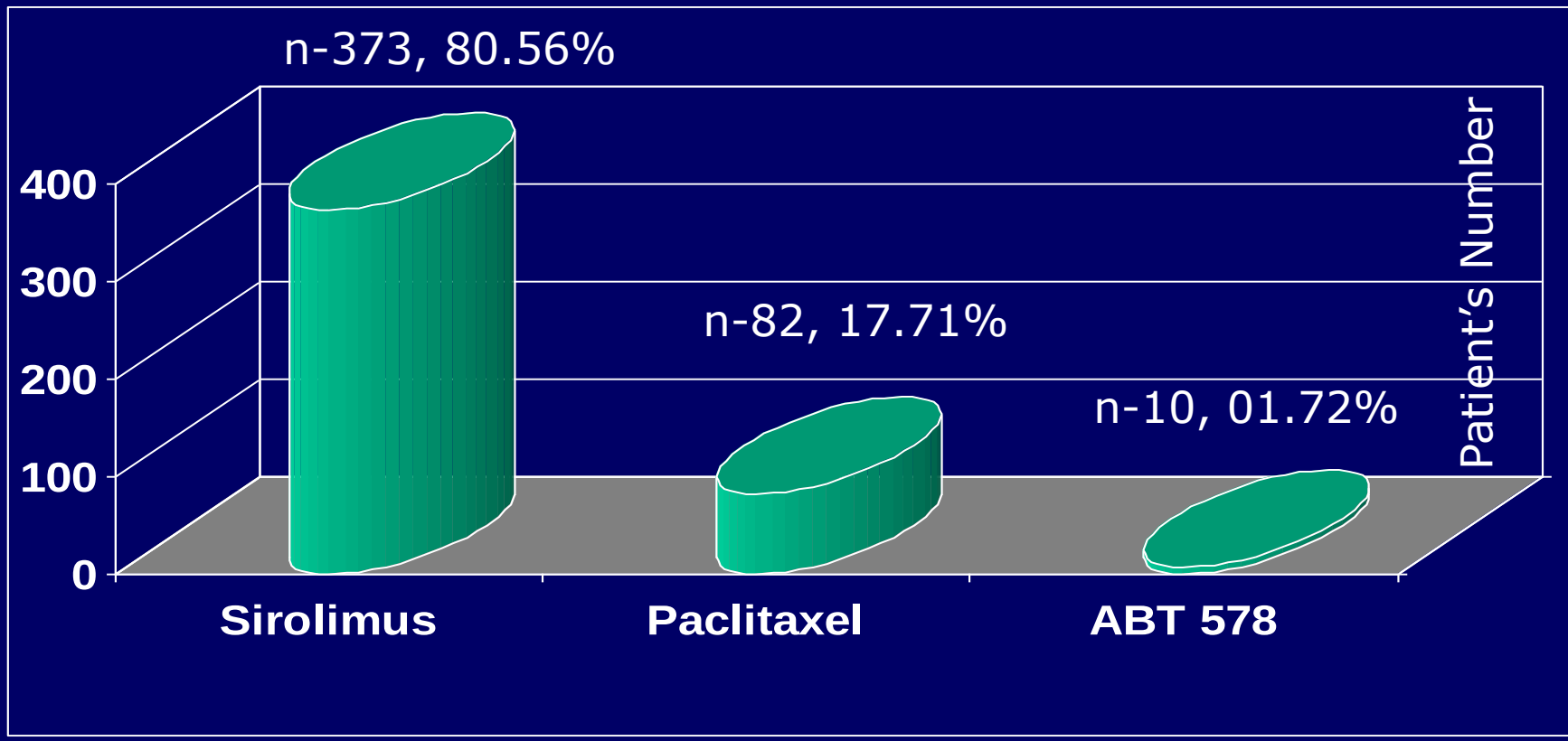
Individual Risk Factors



Indications



Types of DES used



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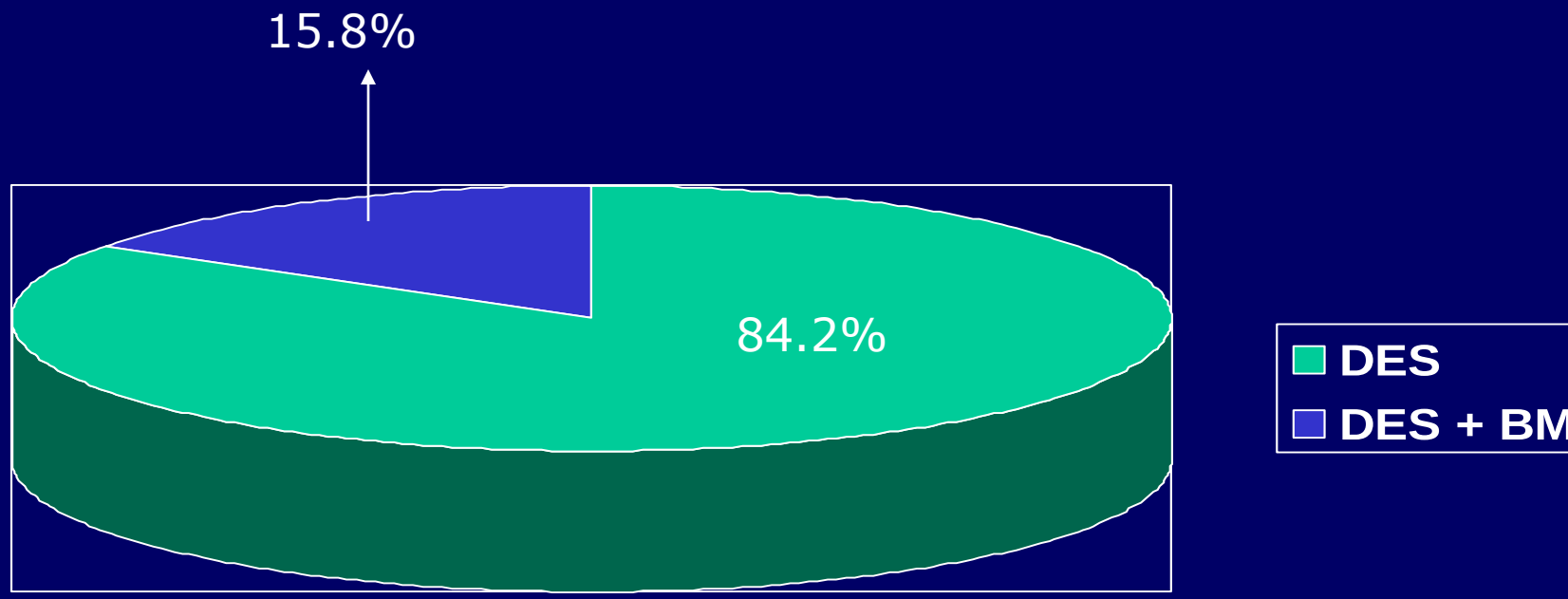
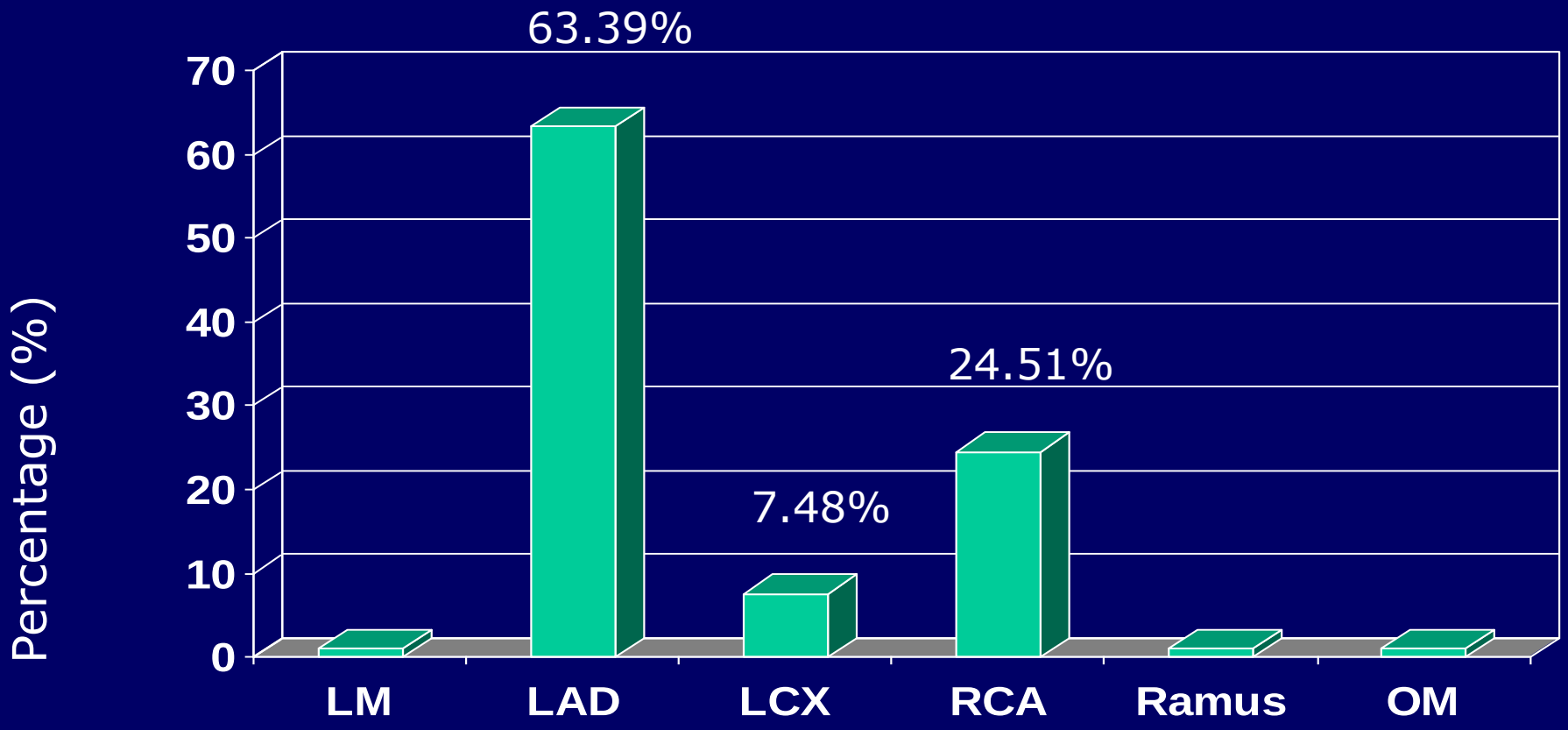
Pattern of Stent Implantation



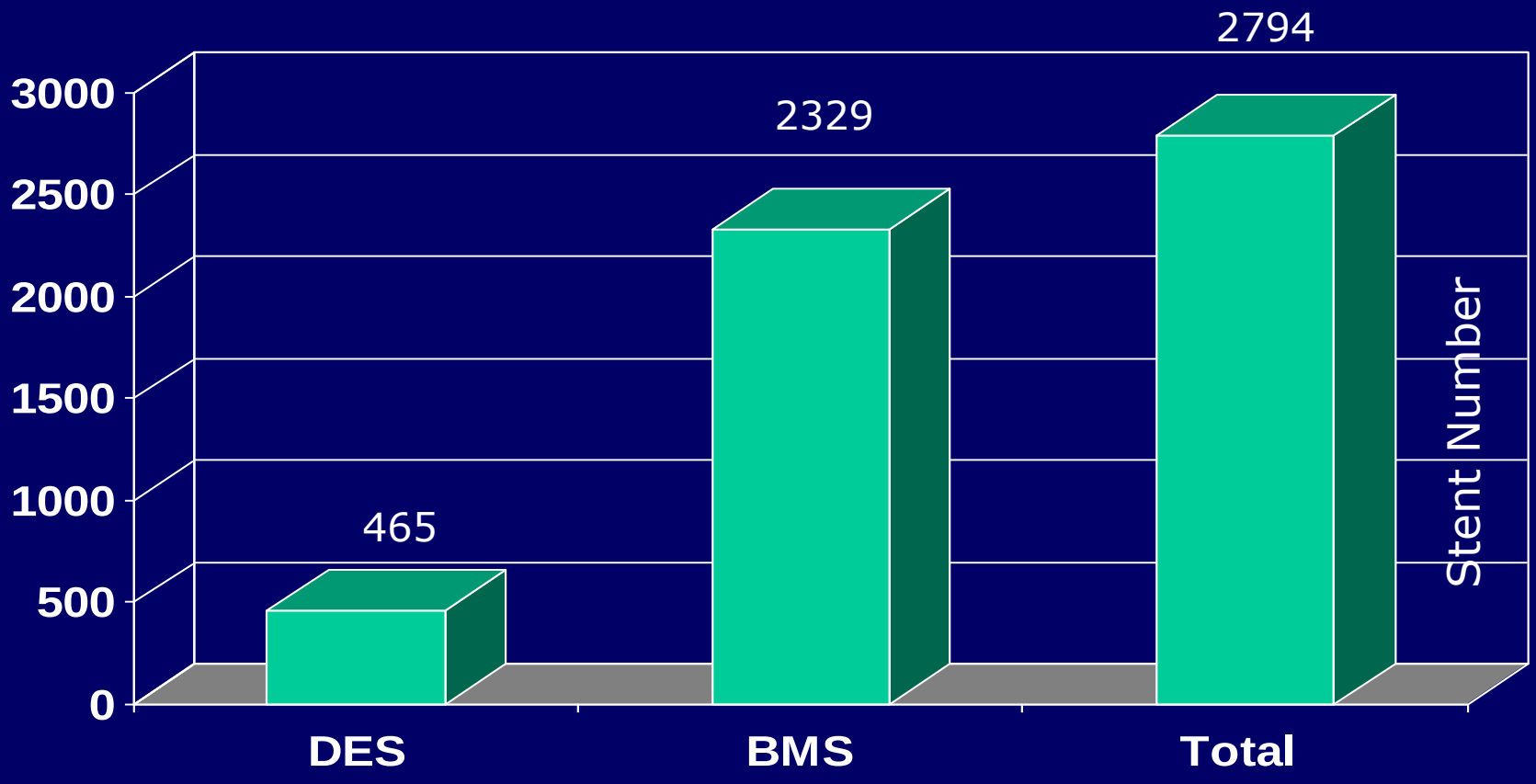
Location of DES



Trends in using DES and BMS

	DES	BMS	Total
2001	0	111	111
2002	2	258	260
2003	13	568	581
2004	135	692	827
2005	292	640	932
Jan, 2006	23	60	83
Total	465	2329	2794

Total use of DES and BMS

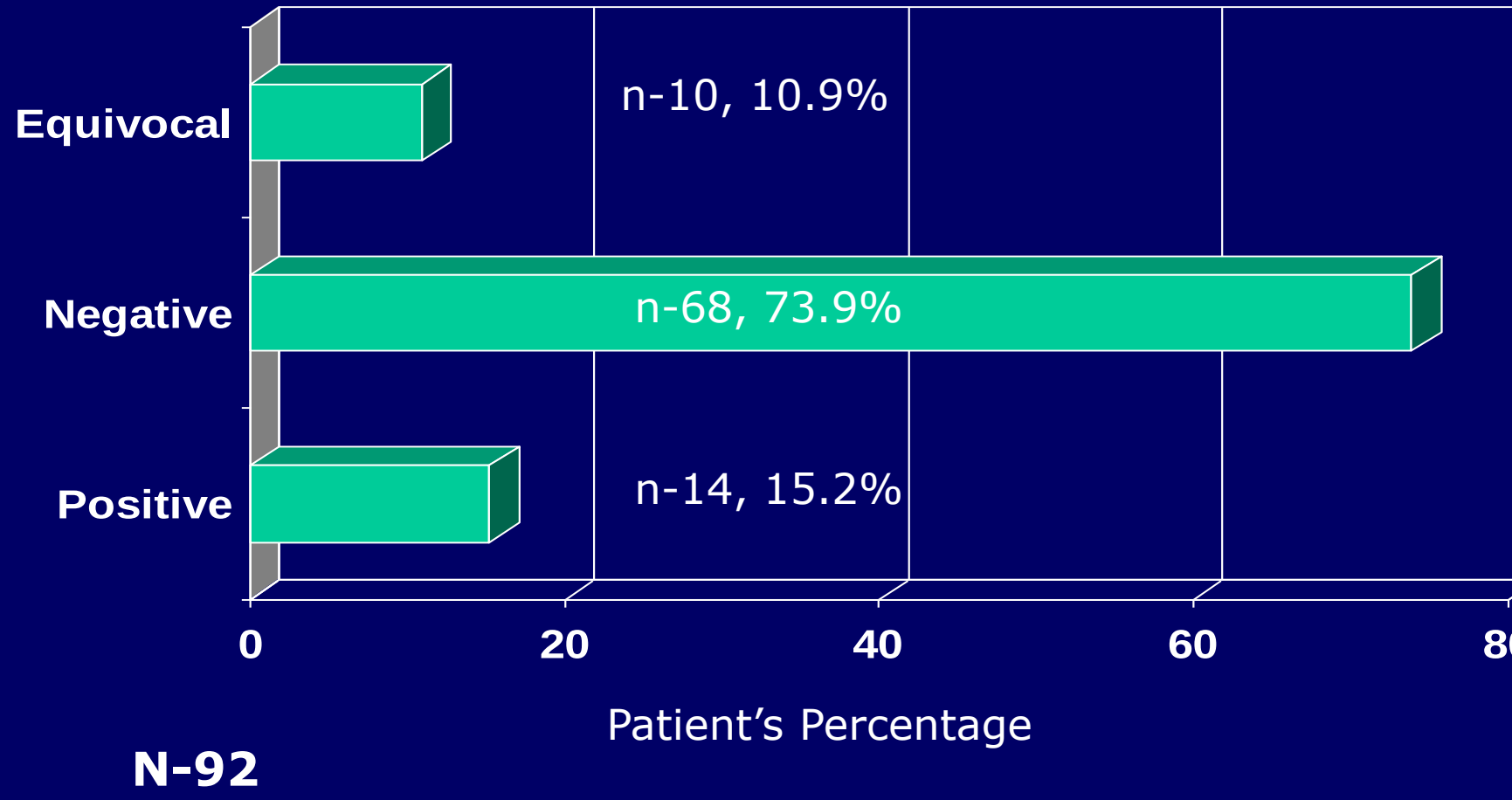


N-2794, DES-465, BMS-2329

OUT COME OF PCI

- TOTAL PATIENT 357
- TOTAL STENT 465
- PROCEDURAL SUCCESS 382 (98%)
- IN HOSPITAL MACE 5 (1.2%)
- IN HOSPITAL DEATH 2 (0.5%)
- MINOR COMPLICATION 15 (3.84%)
- DOCUMENTED ISR 5
- ASYMPTOMATIC 339 (87%)

Follow up ETT pattern



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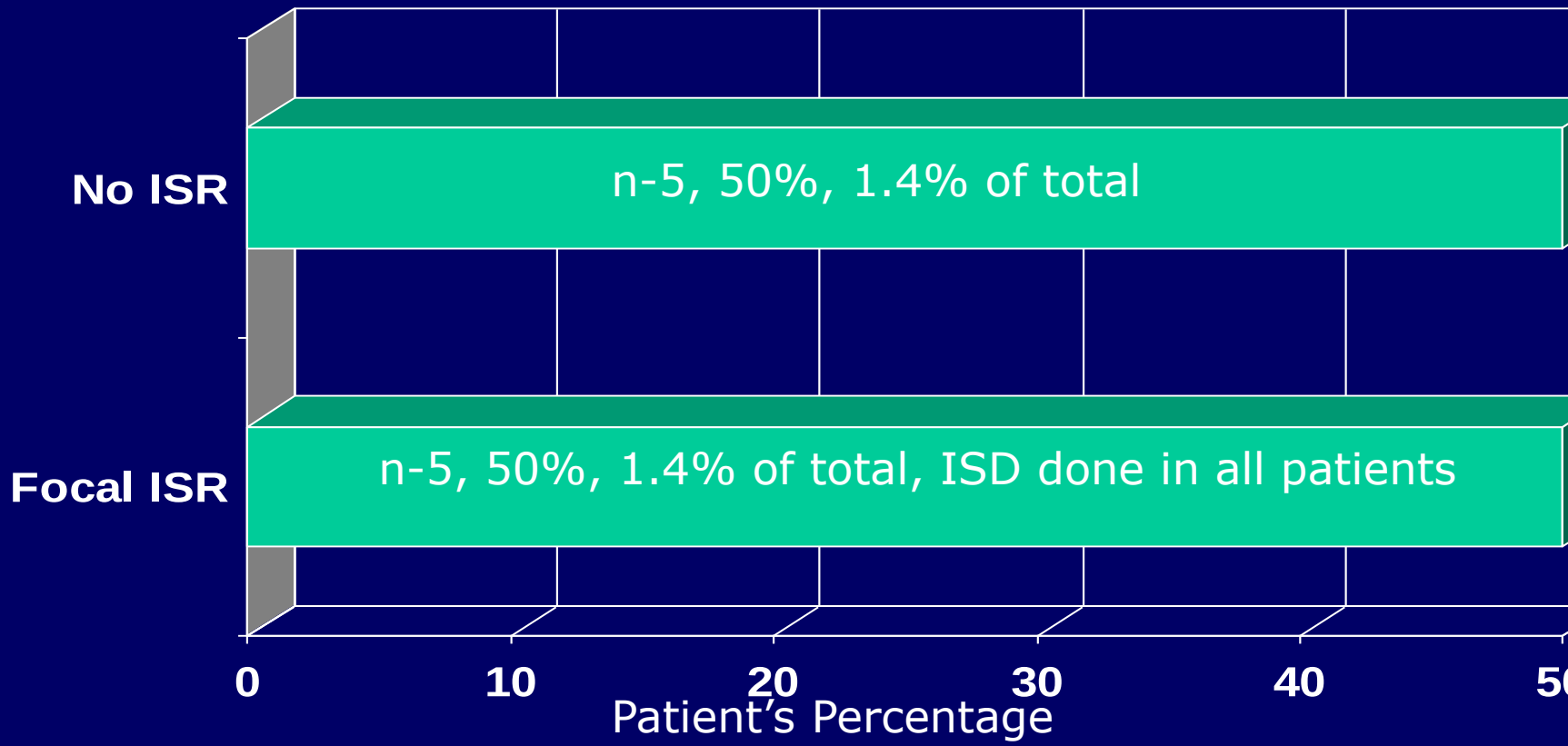
CAG follow up outcome



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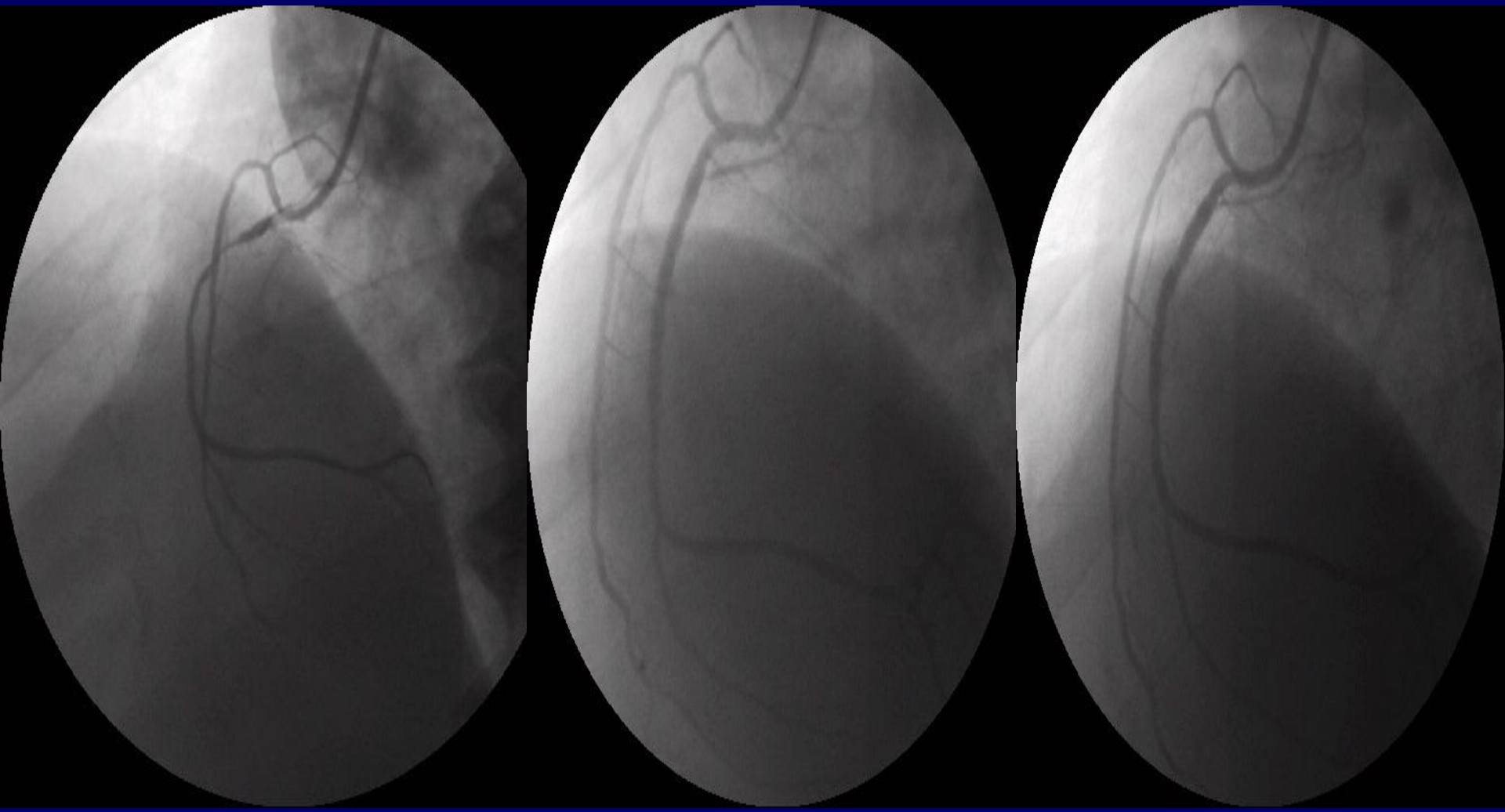

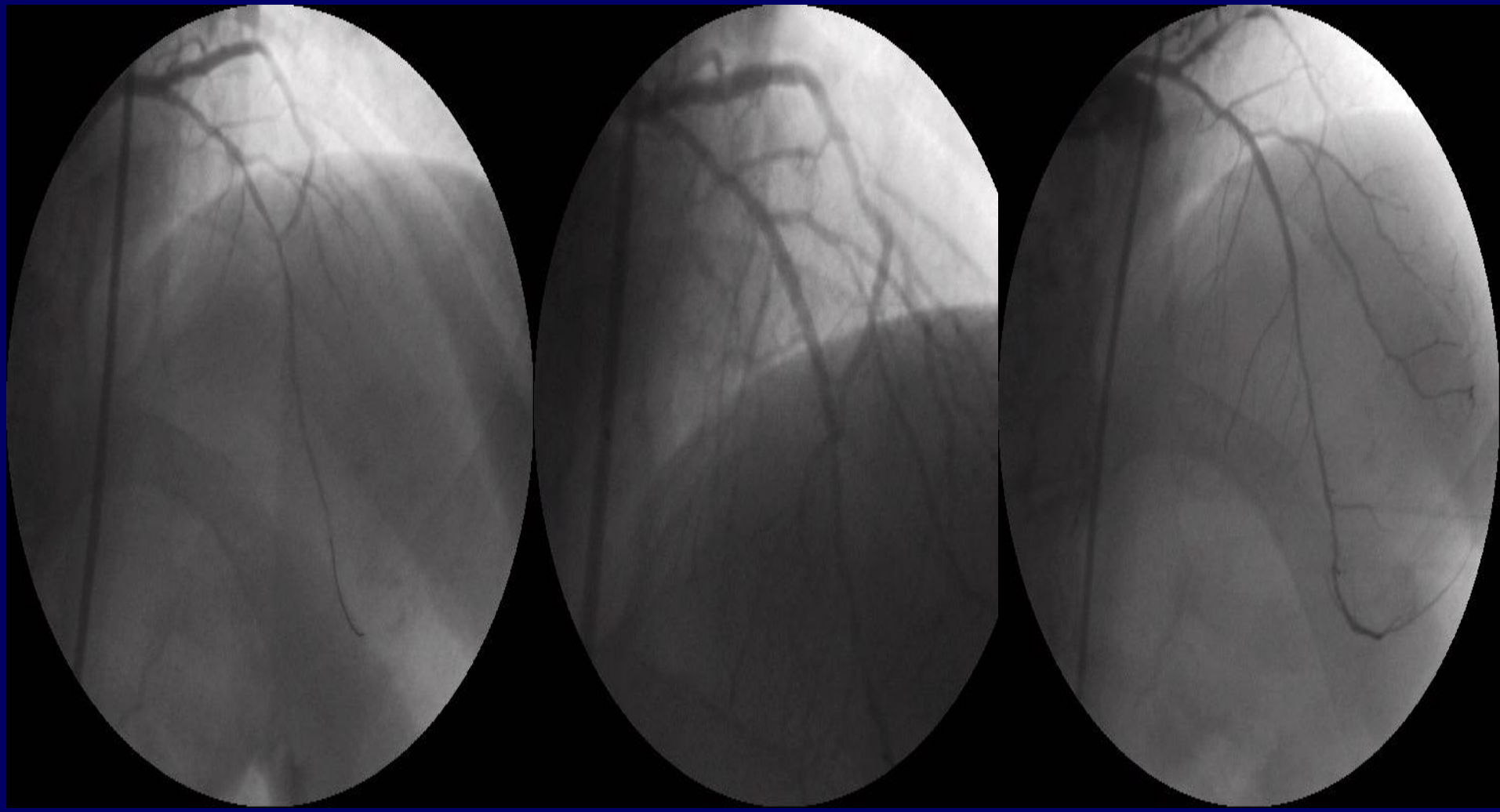

Limitations of previous study

- DES early randomized trials were mostly single lesions, single stents, and excluded high risk patient
- Higher risk profiles, such as diabetes, longer lesions, small or large vessels are too small to derive conclusions on efficacy of DES
- Due to the promise of DES, however, these stents are being placed in many patients excluded from the randomized trials
- There is a need for large, multicenter registries and “focused” clinical trials in these high risk groups to determine the level of efficacy in these patients

Lesions for Which We Need More Data with DES

- Large (>3.5mm) / Small (<2.5mm) Vessels
- Multilesion/Multivessel Intervention (esp in diabetics)
- Saphenous Vein Grafts
- Diffuse Disease (“full metal jackets”)
- Acute MI
- Chronic Total Occlusions
- Bifurcation Lesions
- In-Stent Restenosis
- Restenosis Post-Brachytherapy

Concerns and Controversies

- Safety of DSA coated with potent ant mitotic agents
- Polymers related hazards.
- Accelerated atherosclerosis.
- Delayed stent thrombosis .
- Lack of a long-term effect on restenosis : (>2 years).
- Cost.

CONCLUSION

- Drug Eluting Stents promise to be a huge leap in the treatment of coronary atherosclerotic disease
- It is an emerging technology that has wide scale implications
- Evidence on the clinical efficacy and safety of Drug Eluting Stents is continuously being released
- Given the trend of getting more confidence of intervention cardiologist on DES usage.

Thank You