

**INTERVENTIONAL CARDIOLOGY UPDATE**

# Current Concepts on Revascularization Strategy in Patients with Diabetes Mellitus

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PRESENTATION SLIDES

**ABBREVIATIONS**

BMS = bare metal stent(s)  
CABG = coronary artery bypass grafting  
CAD = coronary artery disease  
CVD = cardiovascular disease  
DES = drug-eluting stent(s)  
DM = diabetes mellitus  
PCI = percutaneous coronary intervention  
RCT = randomized controlled trial

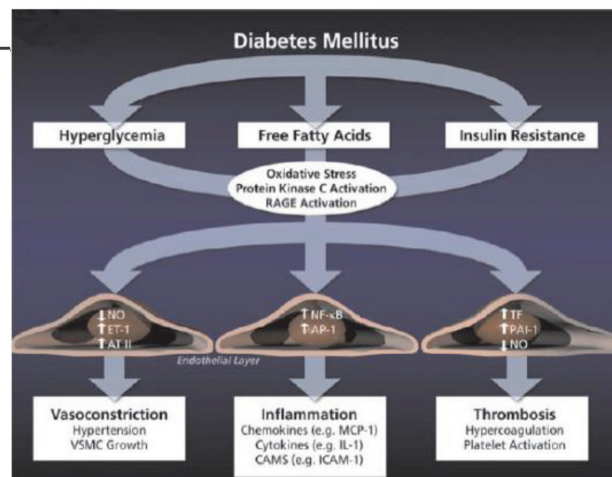
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**Conflict of Interest:** none declared

## Diabetes Mellitus and Epidemiology of CVD

- Estimated 170 million people worldwide suffer from DM
- DM, an atherosclerotic risk equivalent to a history of myocardial infarction
- Threefold to fivefold increased risk of acute coronary events
- 80% of diabetic patients succumb to atherosclerosis related conditions

## Vascular Biology of Diabetes



### CAD in Patients With Diabetes

- More advanced CAD with:
  - Greater plaque burden
  - Longer lesions
  - Smaller, more diffusely diseased vessels
- About 25% of pts undergoing CABG or PCI have DM
- Regardless of the type of revascularization DM pts have a worse prognosis compared to pts without DM
- When it comes to PCI, pts with DM have a higher restenosis rate and are at greater risk for MI and stent thrombosis than pts without DM

### Key issues (Currently unclear) in managing diabetic pts with CAD

- How tight should the glycemic control be (based on HbA1C levels) to decrease the risk for clinical events and improve prognosis?
- Are insulin sensitization medical strategies preferred?
- Is revascularization beneficial?
- What type of revascularization is best?

### Long-term follow up of the UKPDS study. *NEJM 2008; 359:1577*

Trial Period	Intense versus conventional control		Follow-up period	
	First 5 yr, median HbA <sub>1c</sub>	5-10 yr, median HbA <sub>1c</sub>	10-15 yr, median HbA <sub>1c</sub>	15-20 yr, HbA <sub>1c</sub> in final year <sup>2</sup>
Initially Intense	6.6	7.5	8.1	8
Conventional	7.4	8.4	8.7	8.1

Glycemic control contributed 22%, blood pressure control 33% and lipid control 45% to overall long-term outcome

### Glycemic Control and Outcome in DM

- Ultra-tight glycemic control may have adverse rather than beneficial outcome
- Tight blood pressure and lipid control, with tight but not ultra-tight glycemic control seems currently the most appropriate management of pts with DM

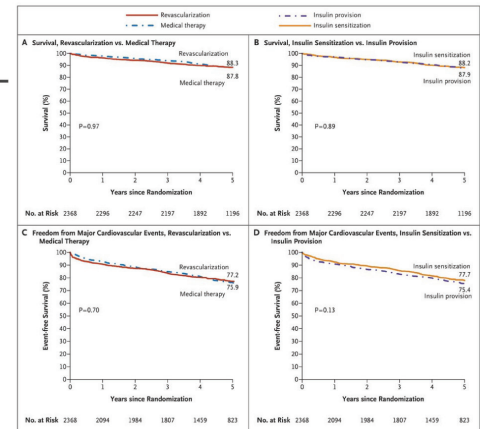
Danish study by Geade et al. *NEJM 2008; 358:580*  
 Long-term follow up of the UKPDS study. *NEJM 2008; 359:1577*  
 ACCORD Trial. *NEJM 2008; 358:2545*  
 ADVANCE Trial. *NEJM 2008; 358:2560*  
 VADT Trial. *NEJM 2009; 360:129*

### BARI 2D Trial

- Multi-center 2X2 factorial RCT
  - Elective Revascularization + Medical Rx versus Medical Rx Only
  - Insulin Sensitization versus Insulin Provision
- 2368 patients with type 2 diabetes and stable CAD
- 5 years follow up
- HbA1C goal <7.0%
- End Points:
  - Primary: All cause mortality (300 expected)
  - Secondary: All cause mortality + non-fatal MI and stroke

The BARI 2D Study Group. *N Engl J Med 2009;360:2503-2515*

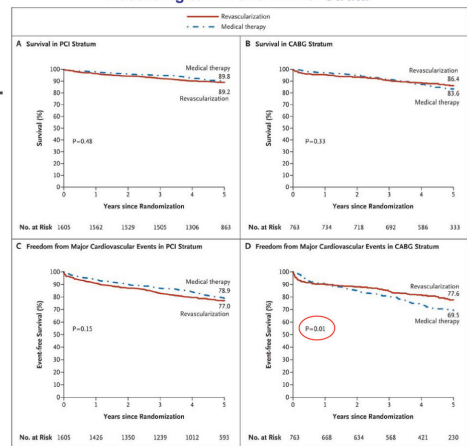
### Rates of Survival and Freedom from Major Cardiovascular Events



The BARI 2D Study Group. *N Engl J Med 2009;360:2503-2515*



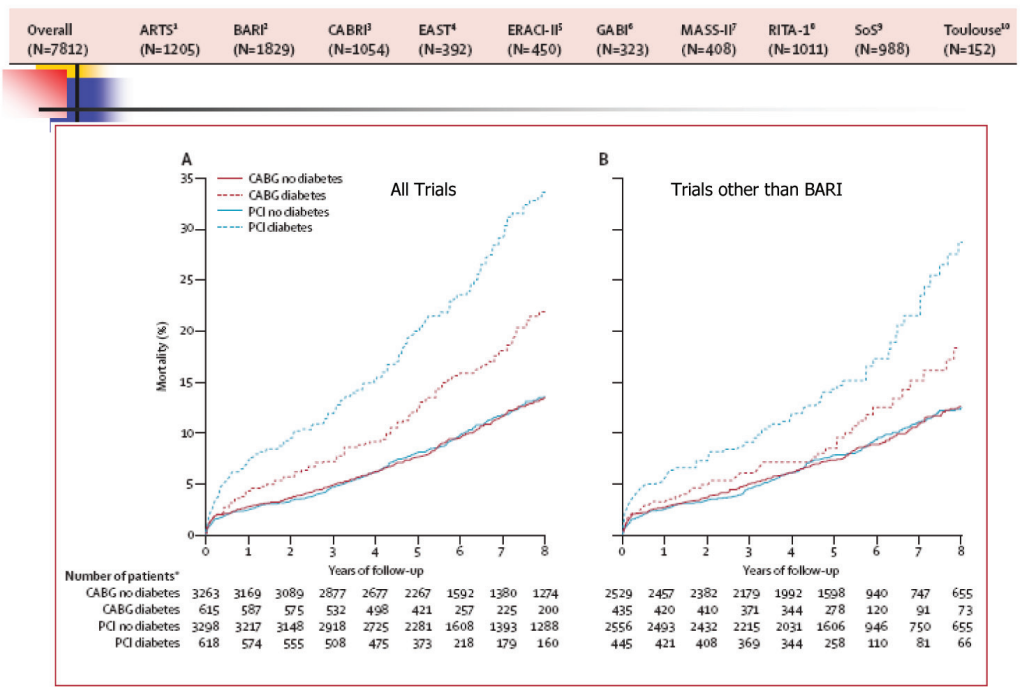
### Rates of Survival and Freedom from Major Cardiovascular Events, According to PCI and CABG Strata



The BARI 2D Study Group. *N Engl J Med 2009;360:2503-2515*



Mortality in Patients Assigned to CABG or PCI by Diabetes Status



SYNTAX Three Year Results in Patients with DM

2. Diabetes – Oral Hypoglycemic vs. Insulin

	Oral Hypoglycemic Agents (N=270)			Insulin (N=182)			Interaction P Value
	CABG (N=128)	PES (N=142)	P Value	CABG (N=93)	PES (N=89)	P Value	
MACCE <sup>a</sup>	22.1% (26)	32.2% (45)	0.07	24.0% (21)	44.5% (39)	0.005	0.33
Death/CVAMI (composite)	14.2% (17)	12.2% (17)	0.59	13.6% (12)	22.7% (20)	0.11	0.13
Death	8.4% (10)	11.5% (16)	0.45	9.1% (8)	17.1% (15)	0.11	0.53
Cardiac death	5.0% (6)	6.5% (9)	0.63	4.5% (4)	12.6% (11)	0.06	
Cerebrovascular accident	5.2% (6)	0.7% (1)	0.03	1.3% (1)	5.2% (4)	0.16	0.03
MI	4.1% (5)	5.8% (8)	0.57	5.7% (5)	5.8% (5)	0.92	0.72
Repeat revascularization	10.1% (11)	24.8% (34)	0.002	16.8% (14)	33.2% (27)	0.02	0.59
PCI	9.4% (10)	22.2% (30)	0.004	13.6% (11)	24.7% (20)	0.05	
CABG	0.8% (1)	4.4% (6)	0.09	3.3% (3)	10.2% (8)	0.11	
Graft Occlusion/Stent thrombosis	3.7% (4)	2.3% (3)	0.52	1.1% (1)	5.8% (5)	0.09	0.10

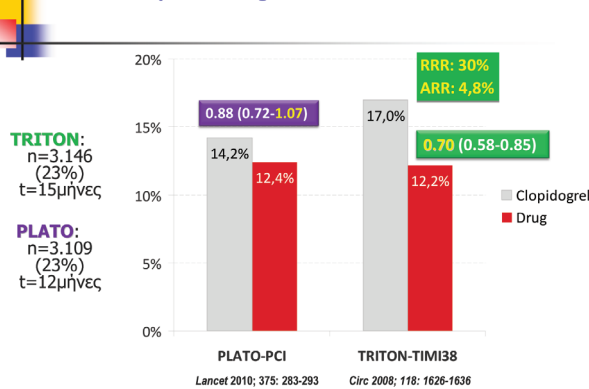
## The Changing Impact of Clinical Trials of Revascularization in Diabetics

**Table 1** Selected Randomized Clinical Trials of Revascularization and Diabetes Mellitus

	Diabetic Patients		All Diabetic Patients
	BARI 353	SYNTAX 452	BARI 2D 2,268
Randomization	PTCA vs. CABG	DES vs. CABG	All revascularization vs. Med Rx
Follow-up reported	10 yrs	1 yr	5 yrs
PCI method	Balloon angioplasty	Taxus DES	35% DES
Patients	Symptomatic multivessel CAD	Symptomatic left main and/or multivessel CAD	Elective, left main excluded
Primary end point	Death 5 yrs	Death, MI, stroke, or revascularization 1 yr	Death 5 yrs
Death	PTCA: 34.5% CABG: 19.4% p = 0.002	DES: 8.4% CABG: 6.4% p = 0.43	All revascularization: 11.7% Med Rx: 12.2% p = 0.97
Death	Not reported	At 1 yr: DES: 10.1% CABG: 10.3% p = 0.96	At 5 yrs: All revascularization: 22.8% Med Rx: 24.1% p = 0.70
Death	Not reported	DES: 26.0% CABG: 14.2% p = 0.003	Not reported
MI	Not reported	Not reported	Not reported
Stroke	Not reported	Not reported	Not reported
Revascularization	Not reported	Not reported	Not reported
Repeat revascularization	PTCA: 69.9% CABG: 11.1% (at 7 yrs)	DES: 20.3% CABG: 6.4%	42% of Med Rx patients crossover to revascularization group p < 0.001
Interaction with anatomic complexity	No	Yes	Not reported

BARI = Bypass Angioplasty Revascularization Investigation; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; DES = drug-eluting stent(s); Med Rx = medical treatment; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angiography; SYNTAX = SYNERgy between percutaneous coronary intervention with TAXus and cardiac surgery.

### New Antiplatelet Agents in Diabetes - PCI



### Characteristics of Current Clinical Practice (Based on the Practice of BARI 2D)

- Investigators could choose between PCI or CABG (as it was the case in the old BARI Registry)
- The majority of diabetic patients with multivessel disease (56%) underwent PCI than CABG
- Among patients assigned to PCI only 49% were deemed equally suitable for CABG
- Among patients selected for CABG only 11% were deemed suitable for PCI
- The study was not designed to compare CABG to PCI

### Conclusions

- Patients with diabetes mellitus who undergo revascularization have a worse outcome compared to non-diabetics regardless of the method of revascularization (CABG or PCI)
- PCI has evolved to an effective method of revascularization even in diabetic patients with multivessel CAD
- There is no short or mid-term death penalty with DES-PCI in diabetic patients, as it was shown in the past with PTCA-BMS/PCI
- The risk or repeat revascularization remains higher in diabetics than non-diabetics despite the DES use, and three fold higher than for patients undergoing CABG