A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease (BARI 2D)
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ClinicalTrials.gov Identifier: NCT00006305

Clinical Question / Statement:
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Optimal treatment for patients with both type 2 diabetes mellitus and stable ischemic heart disease has not been established.

Endpoints:
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Primary: Death from any cause
Secondary: Composite of death, myocardial infarction or stroke (major cardiovascular events)

Enrollment:
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Dates: January 2001 thru March 2005
Sites: USA, Canada, Brazil, Mexico, Czech Republic & Austria
2,368 patients
- 763 CABG stratum
  - 378 randomized to revascularization
    - 188 randomized to insulin sensitization & 190 to insulin provision
  - 385 randomized to medical therapy
    - 191 randomized to insulin sensitization & 194 to insulin provision
- 1605 PCI stratum
  - 798 randomized to revascularization
    - 396 randomized to insulin sensitization & 402 to insulin provision
  - 807 randomized to medical therapy
    - 408 randomized to insulin sensitization & 399 to insulin provision

Inclusion Criteria:
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25 Years & Older
Diagnosis of type 2 diabetes mellitus
Coronary arteriogram showing one or more vessel amenable to revascularization (>= 50% stenosis)
Objective documentation of ischemia or subjective documentation of typical angina with >= 70% stenosis in at least one artery
Ability to perform all tasks related to glycemic control and risk factor management

Exclusion Criteria:
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Definite need for invasive intervention as determined by the attending cardiologist

Prior CABG or PCI within 12 months before study entry
Left main CAD >= 50%
Planned intervention for disease in a bypass graft if the patient was randomly assigned to a strategy of initial revascularization
Class III or IV heart failure
Creatinine of > 2.0 mg/dL
HgbA1c of > 13%
Need for major vascular surgery concomitant with revascularization (Ex. carotid endarterectomy)
Non-cardiac illness expected to limit survival
Hepatic disease (ALT > 2x upper limit of normal)
Fasting triglycerides > 1,000 mg/dL in the presence of moderate glycemic control (HgbA1c of < 9.0%)
Current EtOH abuse
Chronic steroid use judged to interfere with the control of diabetes, exceeding 10 mg of Prednisone per day (or the equivalent)
Pregnancy (known, suspected or planned in 5 years after study entry)
Geographically inaccessible or unable to return for follow-up
Enrolled in a competing randomized trial or clinical study
Unable to understand or cooperate with protocal requirements

Conclusions:
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1) No statistical difference in primary end point between patients undergoing prompt revascularization vs. optimal medical therapy.
2) There may be a trend (statistical difference) in secondary end point between revascularization (CABG stratum) vs. optimal medical therapy (77.6% vs. 69.5%, p = 0.01)
   -Specifically involving the insulin sensitization group vs. the insulin provision group (18.7% vs. 32.0%, p = 0.002)

Criticisms / Discussion:
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-BARI 2D was not designed to be a direct comparison of revascularization strategies and so cannot be generalizable to mean that CABG is superior to PCI among diabetic patients with stable CAD
-No data given on 2,100+ patients who were ineligible for randomization
-"Responsible physician" determined first CABG vs. PCI prior to randomization - PCI cohort may have had less severe CAD than CABG cohort, so inherent selection bias
-Included patients had coronary anatomy amenable to revascularization, limiting generalizability of the results
-High rates of crossover (with repect to both the insulin sensitiation vs. insulin provision metric and the revscularization vs. medical therapy strategies).
-Using CK of 10x the upper limit of normal as the definition of a peri-operative MI may have been too high (most use 5x upper limit of normal).