

What's New in Multivessel Disease?

Insights from Recent Clinical Trials

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Disclosures

Grant Support/Drugs

- Daiichi-Sankyo
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- Eli Lilly
- Astra-Zeneca

Grant Support/Devices

- Edwards Lifesciences
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- Biomet
- Abbott Vascular
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- Covidien

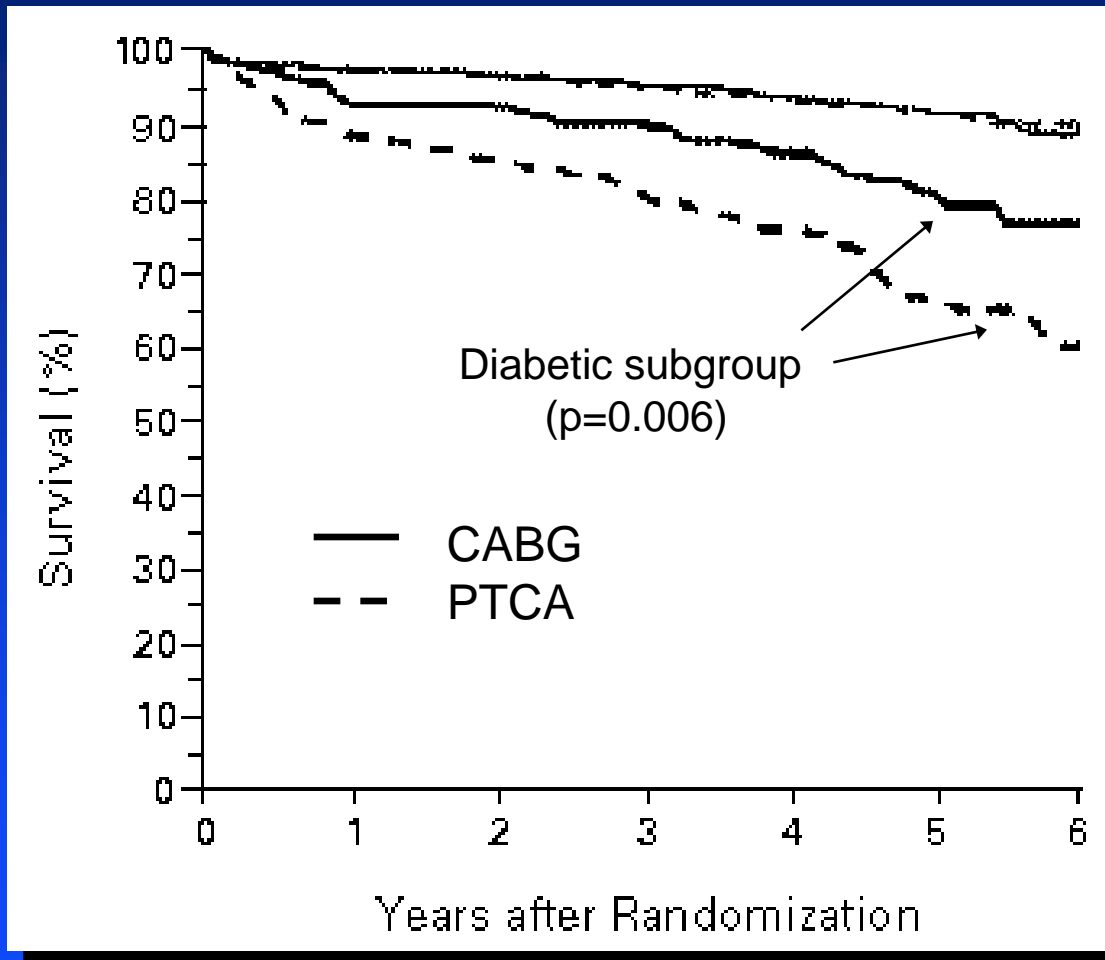
Consulting/Advisory Boards

- Medtronic
- Eli Lilly
- Boehringer-Ingelheim
- Astra-Zeneca

Multivessel Disease Update

Should all patients with diabetes and multivessel CAD undergo CABG?

BARI: Impact of Diabetes on Survival

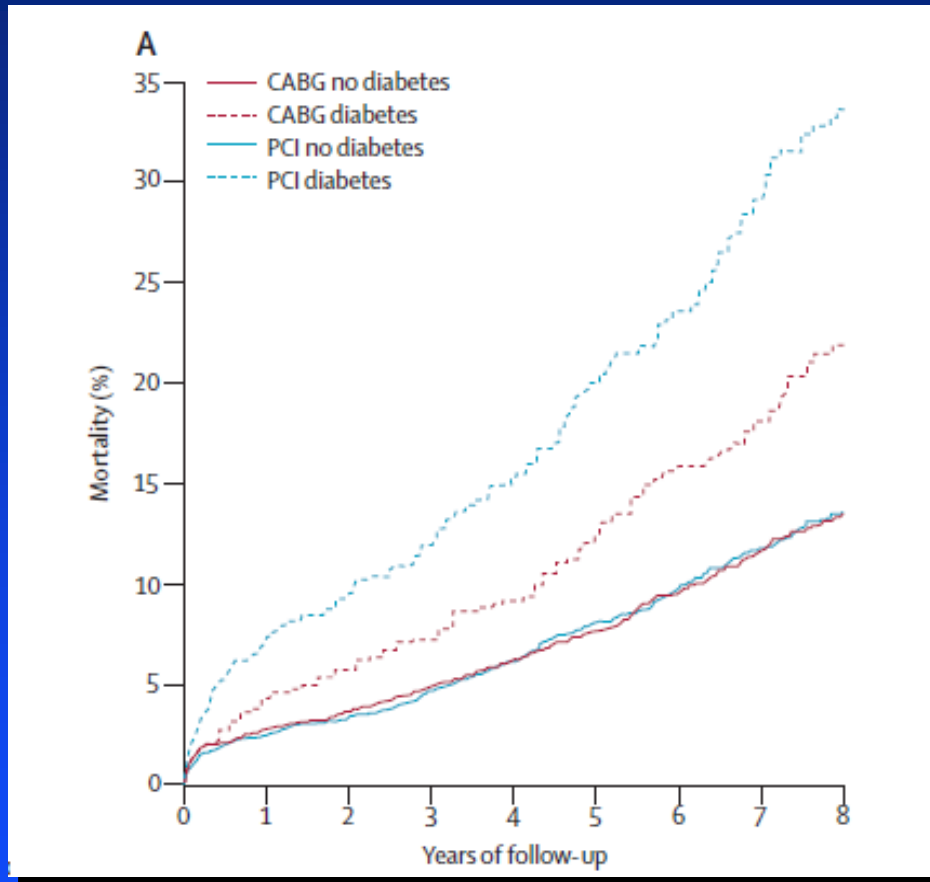


BARI Subgroups

- Treated diabetic pts only subgroup to show significant survival advantage with CABG
- 5 year survival
 - CABG 81%
 - PTCA 65%
- No benefit without LIMA

PCI vs. CABG Meta-Analysis

All-Cause Mortality



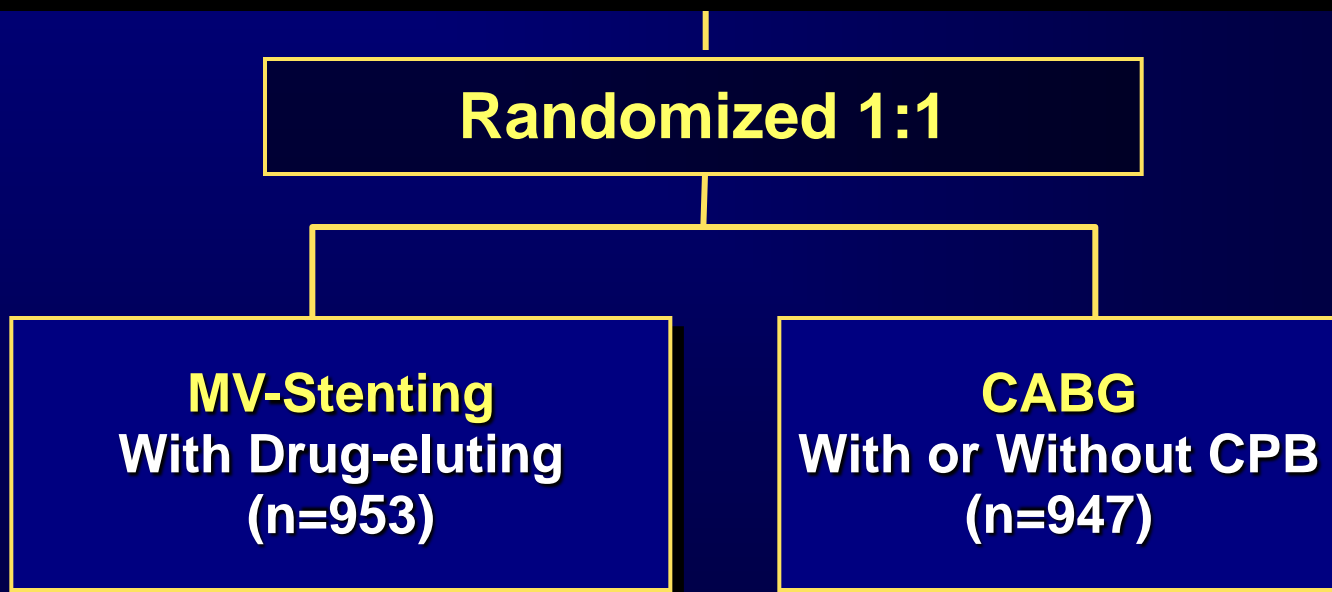
Patient-Level Meta-Analysis

- Pooled individual patient-level data from 10 PCI vs. CABG trials (n=7800)
- Significant interaction ($p=0.014$) between diabetes and survival benefit with CABG
 - No diabetes HR 0.98 (0.86-1.12)
 - Diabetes HR 0.70 (0.56-0.87)
- Similar effect when analysis restricted to stent trials only



FREEDOM Trial

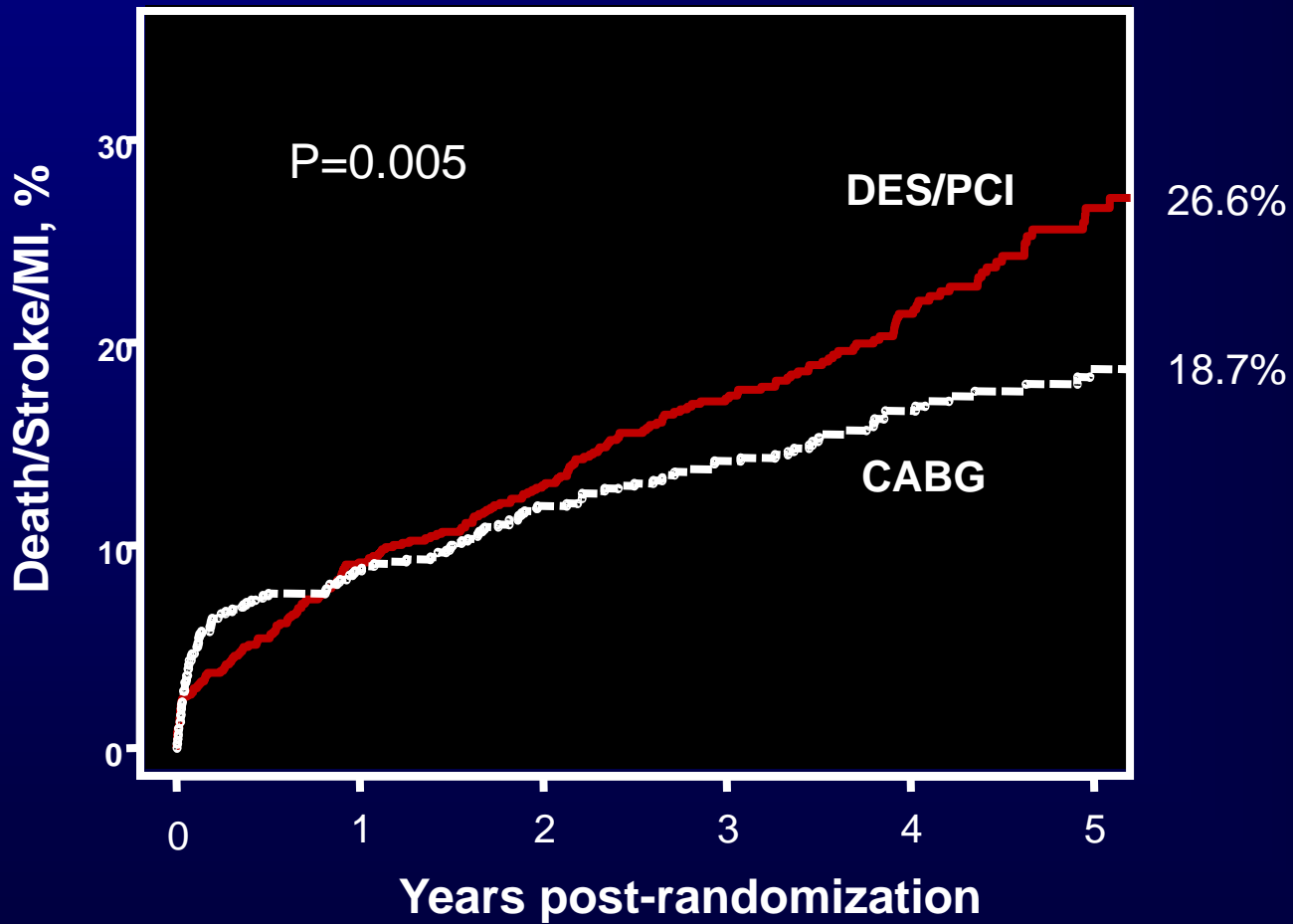
Eligibility: DM patients with MV-CAD eligible for stent or surgery
Exclude: Patients with acute STEMI



All concomitant meds shown to be beneficial were encouraged, including: clopidogrel, ACE inhib., ARBs, B-blockers, statins



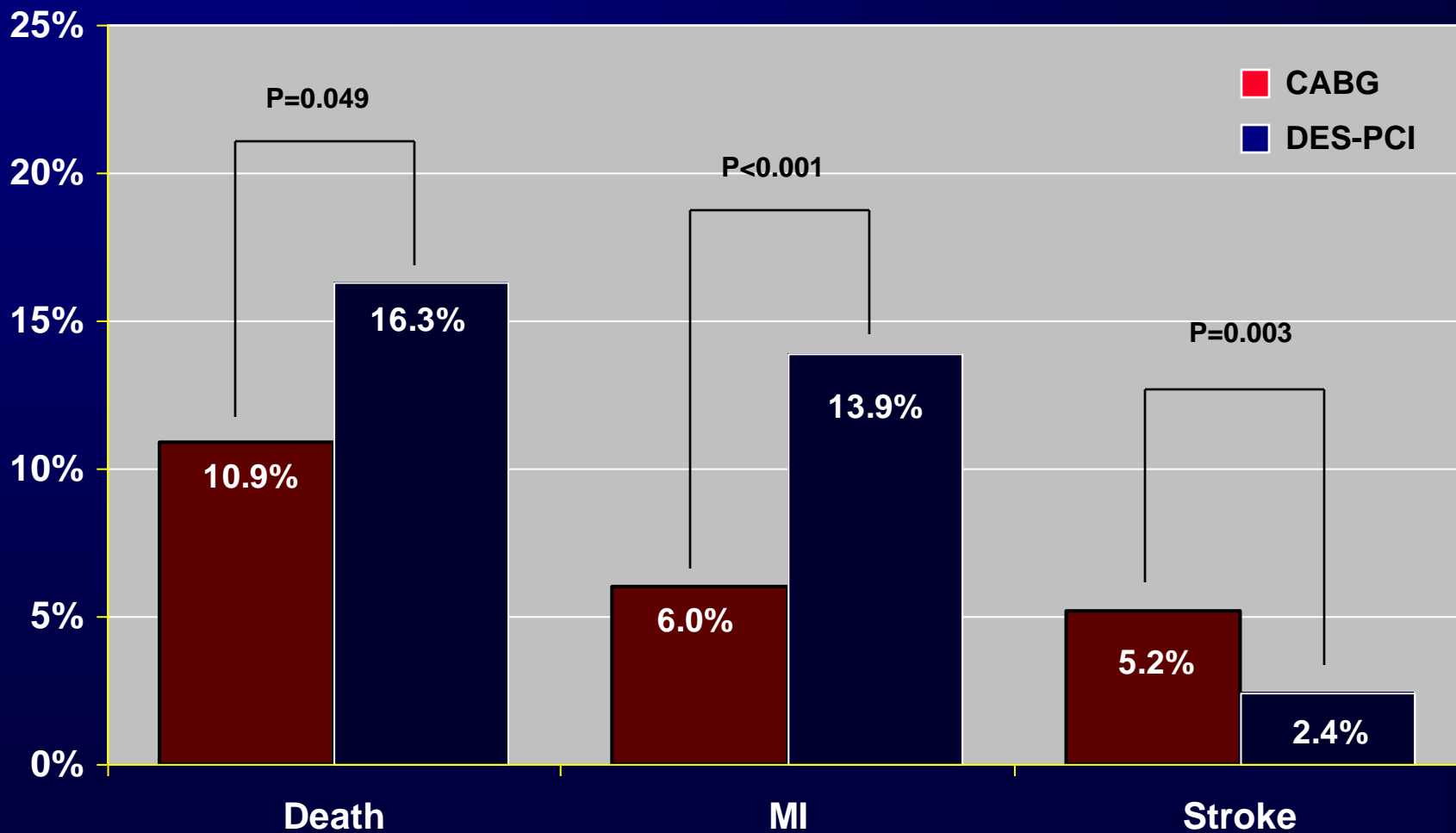
Primary Outcome: Death/Stroke/MI



PCI/DES	953	848	788	625	416	219
CABG	947	814	758	613	422	221

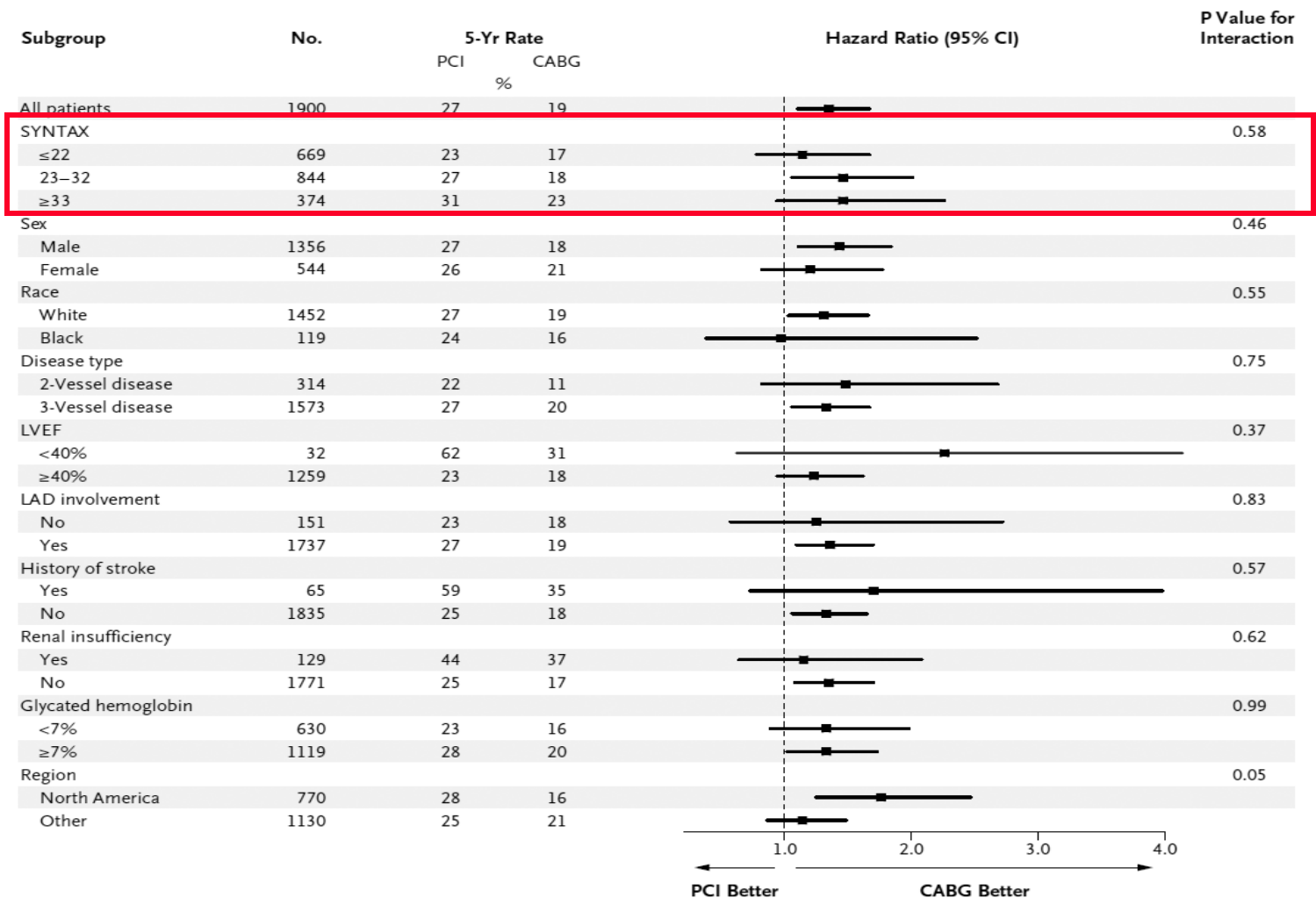


Endpoint Components





Subgroup Analyses: Primary Endpoint



Multivessel Disease Update

*Is FREEDOM the final word on
revascularization in diabetic patients?*

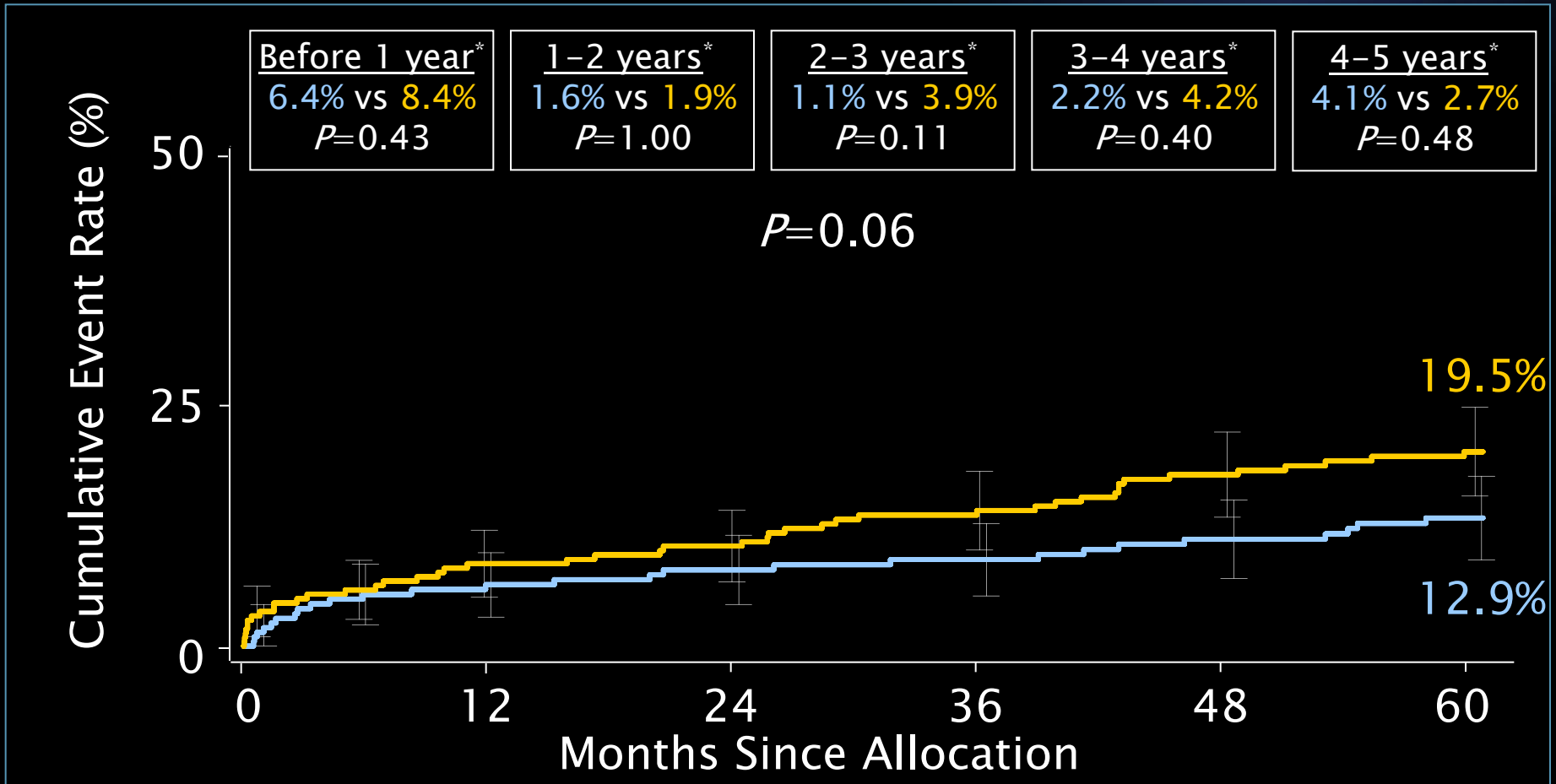
All-Cause Death to 5 Years

Medically-treated Diabetic Subset



■ CABG (N=221)

■ TAXUS (N=231)



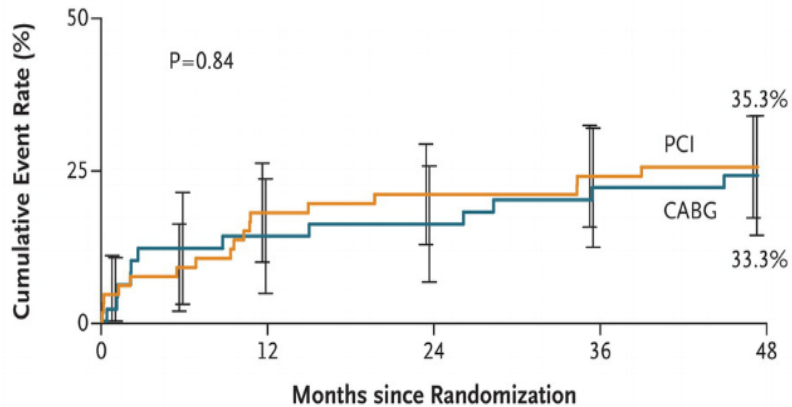
Cumulative KM Event Rate \pm 1.5 SE; log-rank Pvalue; *Binary rates

ITT population

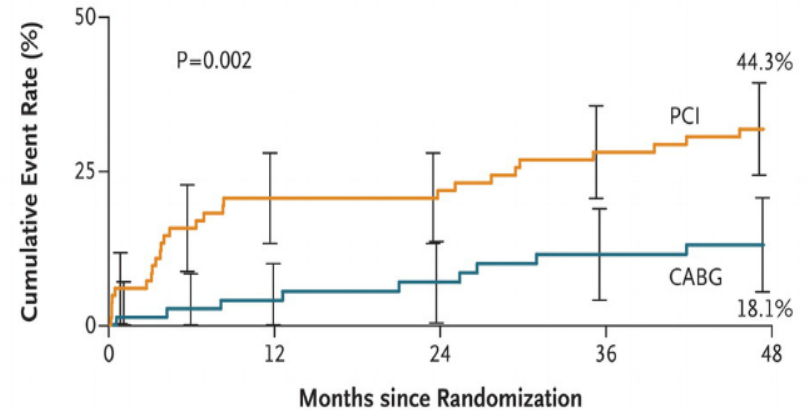
MACCE to 5 Years *Medically-treated Diabetic Subset*



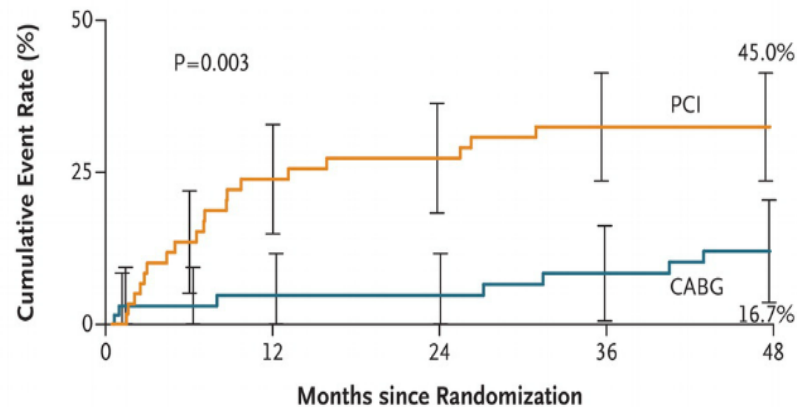
A SYNTAX Score 0–22



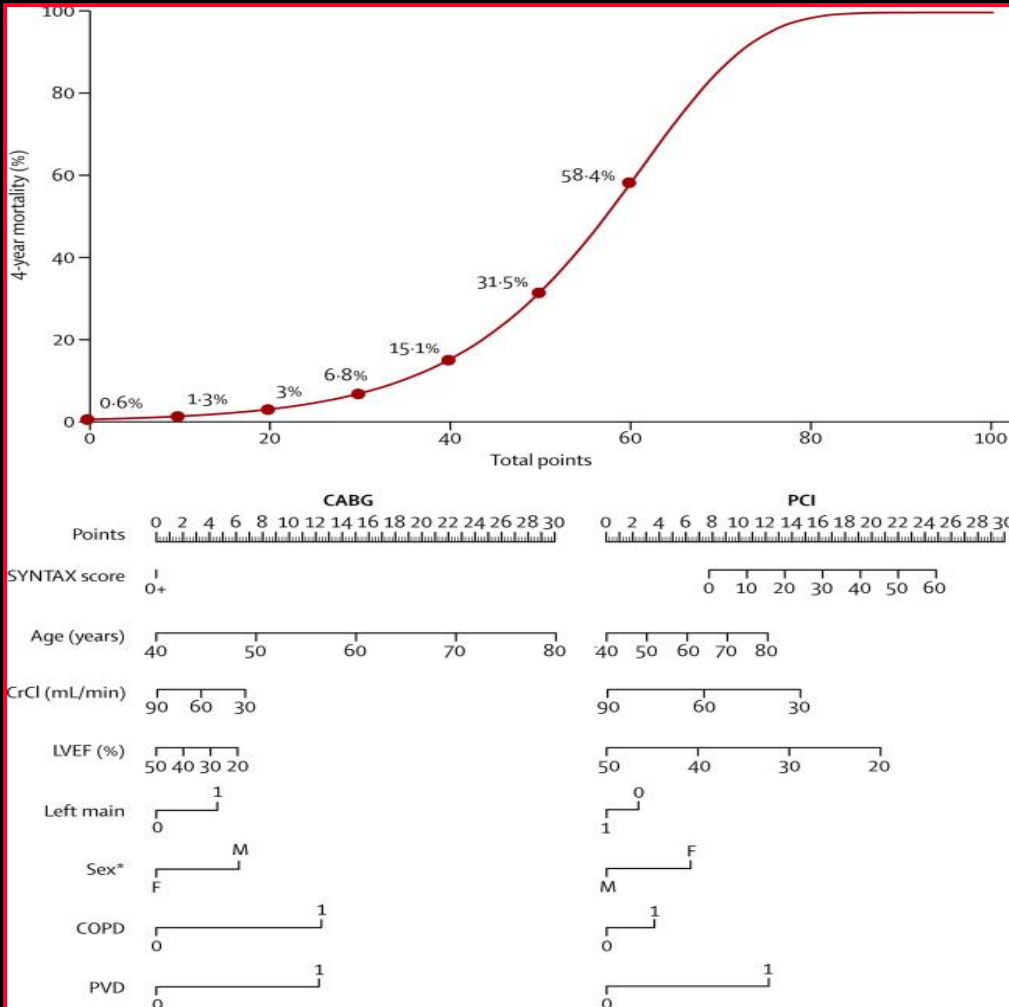
B SYNTAX Score 23–32



C SYNTAX Score ≥ 33



Predictors of 4-Year Mortality SYNTAX Score II



8 Independent Predictors

- Age
- Female Sex
- Creatinine Clearance
- LVEF
- Anatomical SYNTAX Score
- Left main dz
- PAD
- COPD

**After adjustment,
diabetes did not predict
mortality or differential
treatment benefit**

Summary: Revascularization in Pts with Diabetes and Multivessel CAD

- Although FREEDOM demonstrates important benefits of CABG over DES-PCI for both death and MI, these findings do not support a “one size fits all” strategy for diabetic patients
 - *Increased stroke with CABG*
 - *Mortality benefit only emerges after 4-5 years of f/u*
 - *Applies mainly to pts with 3-vessel dz (83% of all pts)*
- SYNTAX suggests that there may be a (small) group of diabetic patients who are at relatively low risk of subsequent events and for whom DES-PCI may still be reasonable → identified based on both anatomic and clinical factors

Multivessel Disease Update

Role of OPCAB– does the approach to CABG matter in 2013?

ROOBY Trial

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On-Pump versus Off-Pump Coronary-Artery Bypass Surgery

A. Laurie Shroyer, Ph.D., Fr
Gerald O. McDonald, M.D.
and Dimitri Novitzky, M.D., Ph.D.,

Trial Design Concerns

- Enrolled low-risk pts (30-day mortality 1.4%)
- Relatively inexperienced surgeons
- Less complete revasc in OPCAB group
- High rate of crossover in OPCAB group (12%)

BACKGROUND

Coronary-artery bypass grafting (CABG) with or without use of cardiopulmonary bypass (on-pump CABG) or off-pump CABG might reduce mortality and improve heart-lung machine.

METHODS

We randomly assigned 2203 patients to on-pump or off-pump procedures. The primary end point was the rate of death or complications (reoperation, stroke, or renal failure) before or after the primary end point. The primary long-term end point was a need for revascularization procedure, or a nonfatal myocardial infarction, or surgery. Secondary end points included mortality at 1 year, neuropsychological

RESULTS

There was no significant difference between the on-pump and off-pump groups in the rate of the 30-day composite outcome (1.4% vs. 1.4%, $P=0.99$) or the rate of the 1-year composite outcome (9.9% vs. 7.4%, $P=0.04$). The rate of revascularization was lower in the off-pump group than in the on-pump group (17.8% vs. 11.1%, $P<0.001$). Fewer patients in the off-pump group underwent 4093 grafts revealed that the mean rate of graft patency was lower in the off-pump group than in the on-pump group (82.6% vs. 87.8%, $P<0.01$). There were no treatment-based differences in neuropsychological outcomes or short-term use of major resources.

CONCLUSIONS

At 1 year of follow-up, patients in the off-pump group had worse composite outcomes and poorer graft patency than did patients in the on-pump group. No significant differences between the techniques were found in neuropsychological outcomes or use of major resources. (ClinicalTrials.gov number, NCT00032630.)

VA Trial

- 2203 pts undergoing isolated CABG randomized to OPCAB

- MI, $P=0.04$
- CV mortality (2.7% vs. 1.3%)
- Repeat revasc (4.6% vs. 3.4%)

CORONARY Trial

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MARCH 28, 2013

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Effects of Off-Pump and On-Pump Coronary-Artery Bypass Grafting at 1 Year

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ABSTRACT

BACKGROUND

Previously, we reported that there was no significant difference at 30 days in the rate of a primary composite outcome of death, myocardial infarction, stroke, or new renal failure requiring dialysis between patients who underwent coronary-artery bypass grafting (CABG) performed with a beating-heart technique (off-pump) and those who underwent CABG performed with cardiopulmonary bypass (on-pump). We now report results on quality of life and cognitive function and on clinical outcomes at 1 year.

METHODS

We enrolled 4752 patients with coronary artery disease who were scheduled to undergo CABG and randomly assigned them to undergo the procedure off-pump or on-pump. Patients were enrolled at 79 centers in 19 countries. We assessed quality of life and cognitive function at discharge, at 30 days, and at 1 year and clinical outcomes at 1 year.

RESULTS

At 1 year, there was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (12.1% and 13.3%, respectively; hazard ratio with off-pump CABG, 0.91; 95% confidence interval [CI], 0.77 to 1.07; $P=0.24$). The rate of the primary outcome was also similar in the two groups in the period between 31 days and 1 year (hazard ratio, 0.79; 95% CI, 0.55 to 1.13; $P=0.19$). The rate of repeat coronary revascularization at 1 year was 1.4% in the off-pump group and 0.8% in the on-pump group (hazard ratio, 1.66; 95% CI, 0.95 to 2.89; $P=0.07$). There were no significant differences between the two groups at 1 year in measures of quality of life or neurocognitive function.

CONCLUSIONS

At 1 year after CABG, there was no significant difference between off-pump and on-pump CABG with respect to the primary composite outcome, the rate of repeat coronary revascularization, quality of life, or neurocognitive function. (Funded by the Canadian Institutes of Health Research; CORONARY ClinicalTrials.gov number, NCT00463294.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Lamy at the Population Health Research Institute, Hamilton Health Sciences, McMaster University, Hamilton, ON L8L 2X2, Canada, or at lamya@mcmaster.ca.

* Deceased.

† Investigators in the CABG Off or On Pump Revascularization Study (CORONARY) are listed in the Supplementary Appendix, available at NEJM.org.

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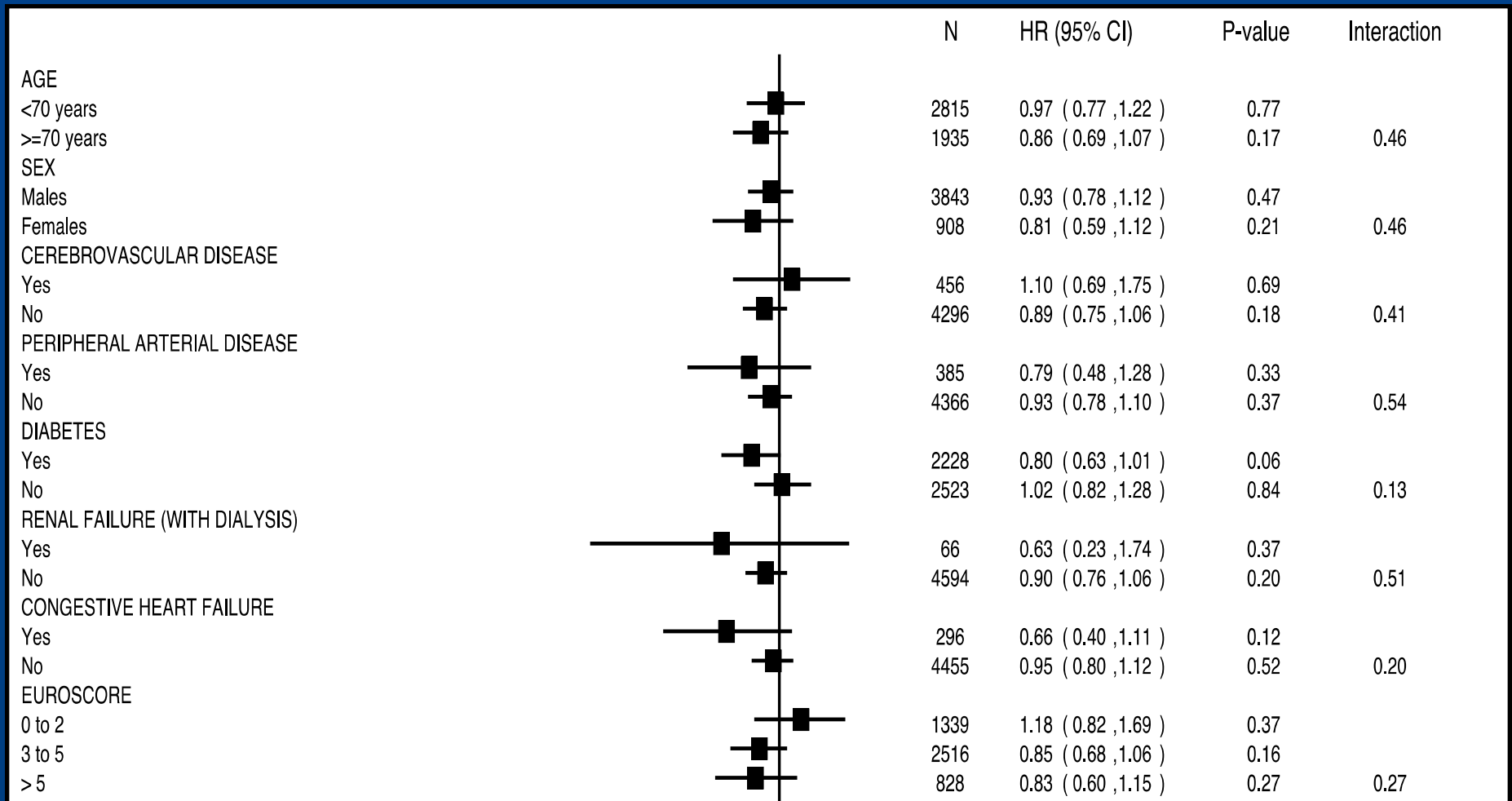
- 4752 patients undergoing CABG with 1 or more risk factors for increased mortality
 - Age > 70
 - Known CVD
 - Recent ACS
 - PAD
 - Diabetes
- Randomized to OPCAB vs. ONCAB
 - Specific surgeons for each procedure
- Primary 1-year endpoint: death, MI, stroke, or renal failure requiring dialysis

1-Year Endpoint Components

	Off Pump %	On Pump %	Hazard Ratio	95% CI	p value
Primary Outcome Death, Stroke, MI, Renal Failure	12.1	13.3	0.91	0.77-1.07	0.24
Components					
Death	5.1	5.0	1.03	0.80-1.32	
Stroke	1.5	1.7	0.90	0.57-1.41	
Non Fatal MI	6.8	7.5	0.90	0.73-1.12	
New Renal Failure	1.3	1.3	0.97	0.59-1.60	

Also no difference with respect to repeat revascularization, QOL, or neurocognitive function

Subgroup Analysis



GOPCABE Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Off-Pump versus On-Pump Coronary-Artery Bypass Grafting in Elderly Patients

Anno Diegeler, M.D., Ph.D., Jochen Börgermann, M.D., Ph.D., Utz Kappert, M.D., Ph.D., Martin Breuer, M.D., Andreas Böning, M.D., Ph.D., Adrian Ursulescu, M.D., Ardawan Rastan, M.D., Ph.D., David Holzhey, M.D., Ph.D., Hendrik Treede, M.D., Ph.D., Friedrich-Christian Rieß, M.D., Ph.D., Philippe Veeckmann, M.D., Amjad Asfoor, M.D., Wilko Reents, M.D., Michael Zacher, M.D., and Michael Hilker, M.D., Ph.D., for the GOPCABE Study Group*

ABSTRACT

BACKGROUND

The benefits of coronary-artery bypass grafting (CABG) without cardiopulmonary bypass in the elderly are still undetermined.

METHODS

We randomly assigned patients 75 years of age or older who were scheduled for elective first-time CABG to undergo the procedure either without cardiopulmonary bypass (off-pump CABG) or with it (on-pump CABG). The primary end point was a composite of death, stroke, myocardial infarction, repeat revascularization, or new renal-replacement therapy at 30 days and at 12 months after surgery.

RESULTS

A total of 2539 patients underwent randomization. At 30 days after surgery, there was no significant difference between patients who underwent off-pump surgery and those who underwent on-pump surgery in terms of the composite outcome (7.8% vs. 8.2%; odds ratio, 0.95; 95% confidence interval [CI], 0.71 to 1.28; $P=0.74$) or four of the components (death, stroke, myocardial infarction, or new renal-replacement therapy). Repeat revascularization occurred more frequently after off-pump CABG than after on-pump CABG (1.3% vs. 0.4%; odds ratio, 2.42; 95% CI, 1.03 to 5.72; $P=0.04$). At 12 months, there was no significant between-group difference in the composite end point (13.1% vs. 14.0%; hazard ratio, 0.93; 95% CI, 0.76 to 1.16; $P=0.48$) or in any of the individual components. Similar results were obtained in a per-protocol analysis that excluded the 177 patients who crossed over from the assigned treatment to the other treatment.

CONCLUSIONS

In patients 75 years of age or older, there was no significant difference between on-pump and off-pump CABG with regard to the composite outcome of death, stroke, myocardial infarction, repeat revascularization, or new renal-replacement therapy within 30 days and within 12 months after surgery. (Funded by Maquet; GOPCABE ClinicalTrials.gov number, NCT00719667.)

From Herz- und Gefäß-Klinik Bad Neustadt, Bad Neustadt (A.D., W.R., M.Z.), Herz- und Diabeteszentrum Bad Oeynhäuser, Bad Oeynhäuser (J.B.), Herzzentrum Dresden, Dresden (U.K.), Universitätsklinik Jena, Jena (M.B.), Universitätsklinik Giessen, Giessen (A.B.); Robert Bosch Krankenhaus Stuttgart, Stuttgart (A.U.), Herzzentrum Universität Leipzig, Leipzig (A.R., D.H.), Universitätsklinik Hamburg-Eppendorf (H.T.) and Albertinen-Krankenhaus Hamburg (F.-C.R.), Hamburg, Klinikum für Herzchirurgie Karlsruhe, Karlsruhe (P.V.), Universität Bochum, Bochum (A.A.), and Universitätsklinik Regensburg, Regensburg (M.H.) — all in Germany. Address reprint requests to Dr. Diegeler at Cardiovascular Clinic Bad Neustadt, Salzburger Leite 1, 97616 Bad Neustadt, Germany, or at cchir@herzchirurgie.de.

*A complete list of investigators in the German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients (GOPCABE) study is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Diegeler, Reents, and Zacher contributed equally to this article.

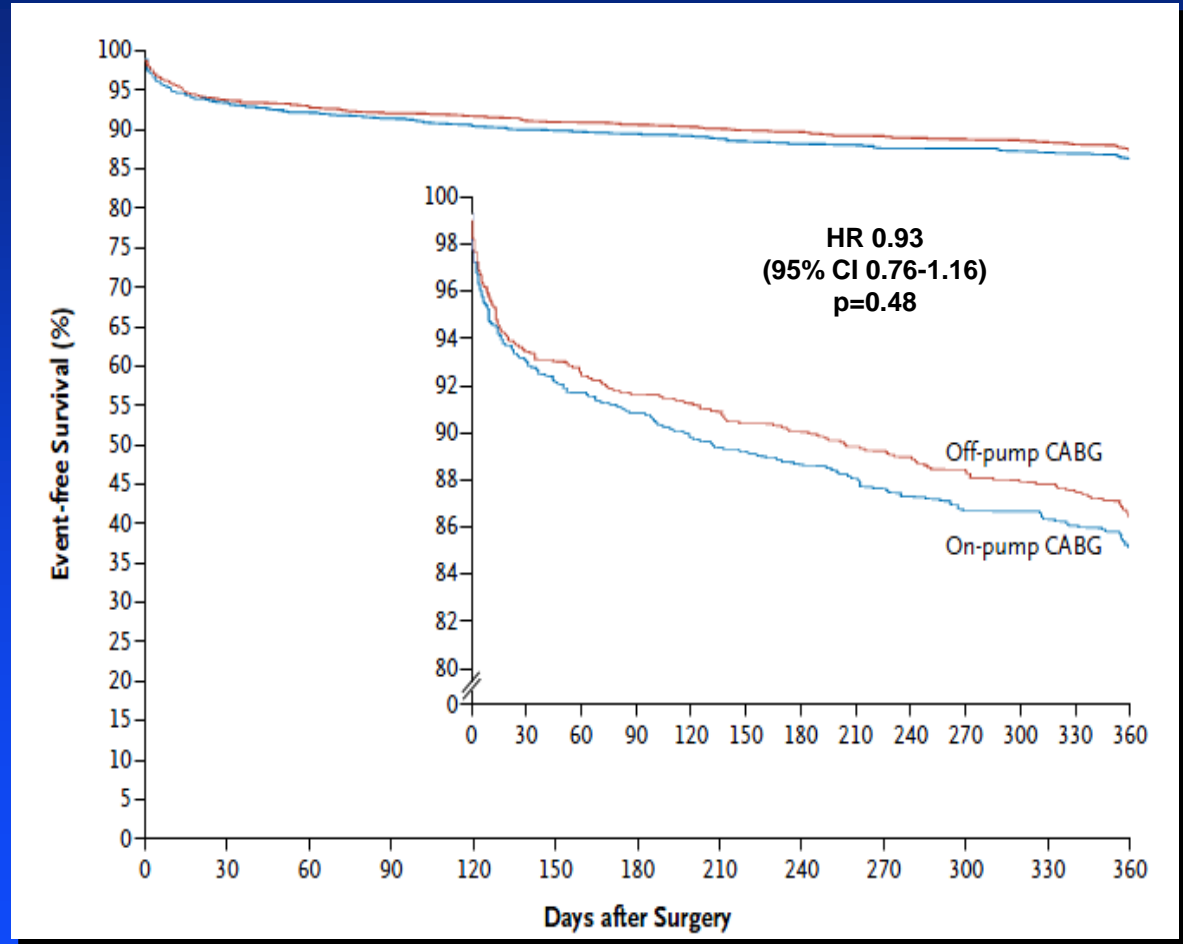
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- 2539 elderly patients (age >75) undergoing elective first-time CABG randomized to OPCAB vs. ONCAB
- Patients enrolled at 12 German centers selected for experience with OPCAB (avg 544 procedures)
- Primary endpoint: death, MI, stroke, new dialysis, repeat revasc at 30 days and 1-year

Primary Endpoint

Freedom from Death, MI, Stroke, Dialysis, Revasc



- No difference in primary endpoint (13.1% vs. 14.0%) or individual endpoint components
- Weak trends toward reduced mortality (7.0 vs. 8.0%) and stroke (3.5% vs. 4.4%) with OPCAB

Summary: OPCAB vs. Standard CABG

- No clear evidence of reduced mortality in moderate risk patients, even with experienced surgeons
- OPCAB does appear to provide a modest reduction in stroke and transfusion, at the expense of increased repeat revascularization
- For most patients, there is no strong reason to recommend one or the other surgical approach → select approach based on patient preference and surgical expertise