CABG vs PCI
The evidence

November 2008

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CABG: a great success story

- Alexis Carrel (1872 to 1944) understood the association between angina pectoris and coronary stenosis (2).
- Coronary surgery moved into the modern era in the 1950s.It is not entirely clear to whom credit should be given for the first coronary bypass. The first direct surgical approach to the coronary circulation in a patient was likely performed by William Mustard in 1953 in Toronto, who used a carotid-to coronary bypass. The patient did not survive the operation.
- The first clinical use of the IMA to graft a coronary vessel appears to have been in response to an intraoperative misadventure.William Longmire applied the technique of coronary endarterectomy in a series of patients in 1958. A right coronary artery disintegrated during one of these operations,and an IMA was placed as a direct graft to restore flow. In retrospect, the surgeon thought it to be a good operation.
- Michael DeBakey and Edward Garrett had a similar experience with a left anterior descending (LAD) coronary endarterectomy in 1964. This situation was salvaged by an aortocoronary saphenous vein graft. The patient did well and had a patent aortocoronary SVG when restudied 8 years later.
- An aortocoronary SVG operation by David Sabiston at Duke in 1962, involving an anastomotic end-to-end technique done without the use of CPB, was the first planned saphenous vein operation but was complicated by an early fatal outcome.

1950s

- Mason Sones showed the feasibility of selective coronary arteriography and amassed a large library of cineangiograms that were studied in depth by Rene Favaloro. Sones and Favaloro formed an innovative team that demonstrated the efficacy and safety of SVG interposition and aortocoronary SVGs for single-vessel, left main, and multivessel coronary disease. An explosive growth in the application of these techniques ensued, such that within a decade, coronary bypass operation became the most frequent surgical procedure in the United States.
- Recognition of the value of the IMA as a conduit came slowly. V.I.Kolessov, working in the 1960s at the Pavlov Institute in Leningrad, described a series of patients in whom the IMA was used for coronary revascularization without the aid of routine arteriography or CPB.

1960s

- After preliminary animal and cadaveric work with microscopic methods, George Green brought this technique to successful clinical application.
- Floyd Loop and colleagues at the Cleveland Clinic incorporated the IMA into the coronary operation in a large series of patients and subsequently published the landmark article demonstrating the powerful survival benefit afforded by use of the IMA for LAD coronary distribution revascularization.

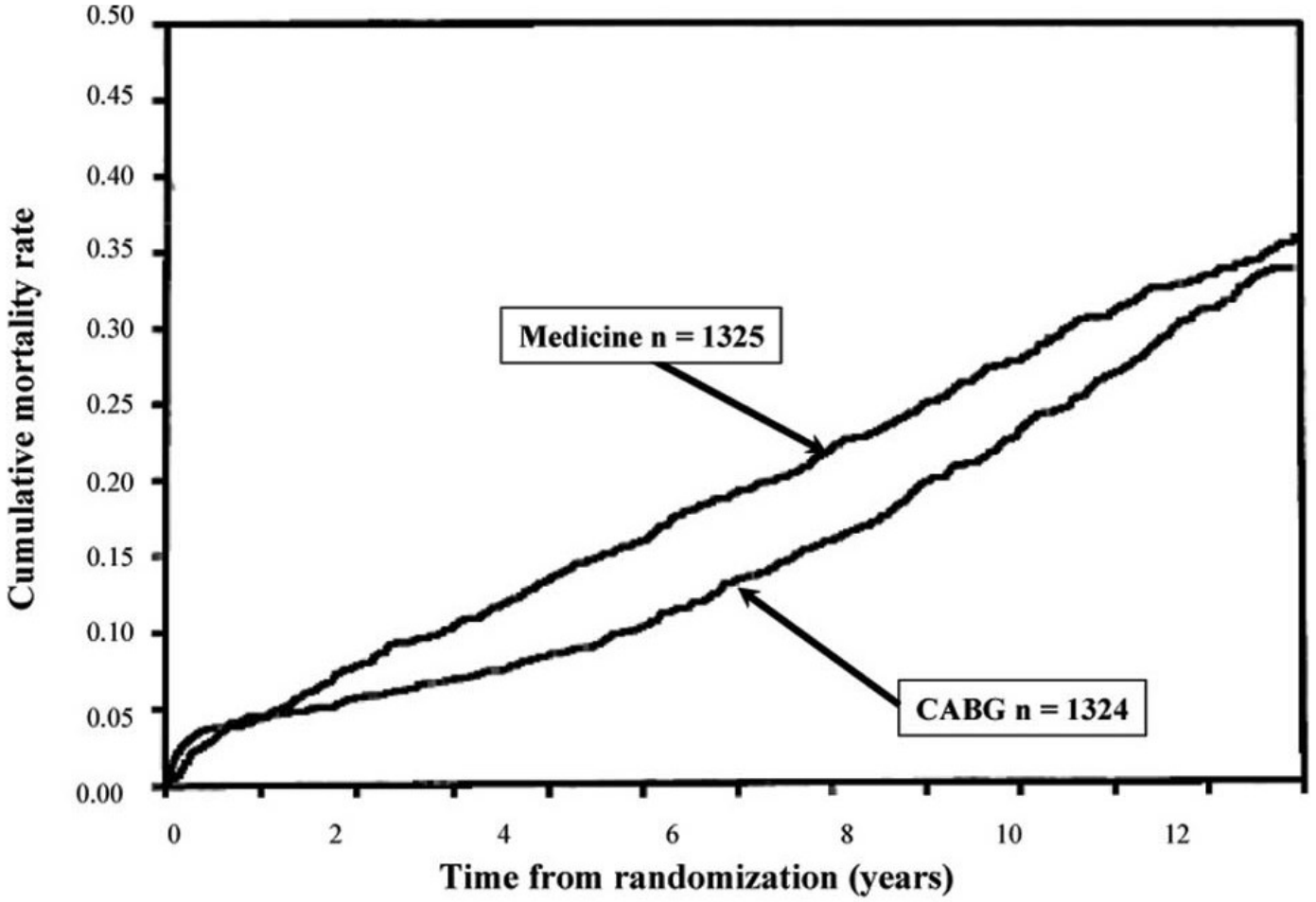
1970s

- The 1970s, the first full decade of CABG, helped to define its appropriate role relative to medical therapy. Coronary bypass was found to consistently relieve angina and improve the quality of life in symptomatic patients.
- Three large, prospectively randomized, multicenter trials, The Coronary Artery Surgery Study (CASS), The Veteran's Administration Coronary Artery Bypass Trial, and the European Coronary Artery Bypass Trial, were conducted.

1980s

- Anesthetic techniques, CPB technology,and most important, methods of myocardial protection were refined and successfully applied to specific problem situations. Close collaboration between the surgeon, the anesthesiologist, the perfusionist, and the intensive care team has been critically important to these advances.
- These refinements have led to an expected 30-day mortality of less than 1% in patients receiving elective coronary bypass who are less than 65 years of age and who have no severe LV dysfunction or congestive heart failure. Even in otherwise uncomplicated patients aged less than 65 years and with an ejection fraction (EF) of 0.25 to 0.35, first-time coronary bypass has an operative mortality risk of less than 5%.

CABG vs medical therapy



Levels of evidence and classification of recommendations

- **Classification of Recommendations**
- **Class I:** Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
- **Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
- **Class IIa:** Weight of evidence/opinion is in favor of usefulness/efficacy.
- **Class IIb:** Usefulness/efficacy is less well established by evidence/opinion.
- **Class III:** Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

- **Level of Evidence**
- **Level of Evidence A:** Data derived from multiple randomized clinical trials or meta-analyses.
- **Level of Evidence B:** Data derived from a single randomized trial, or nonrandomized studies.
- **Level of Evidence C:** Only consensus opinion of experts,case studies, or standard-of-care.

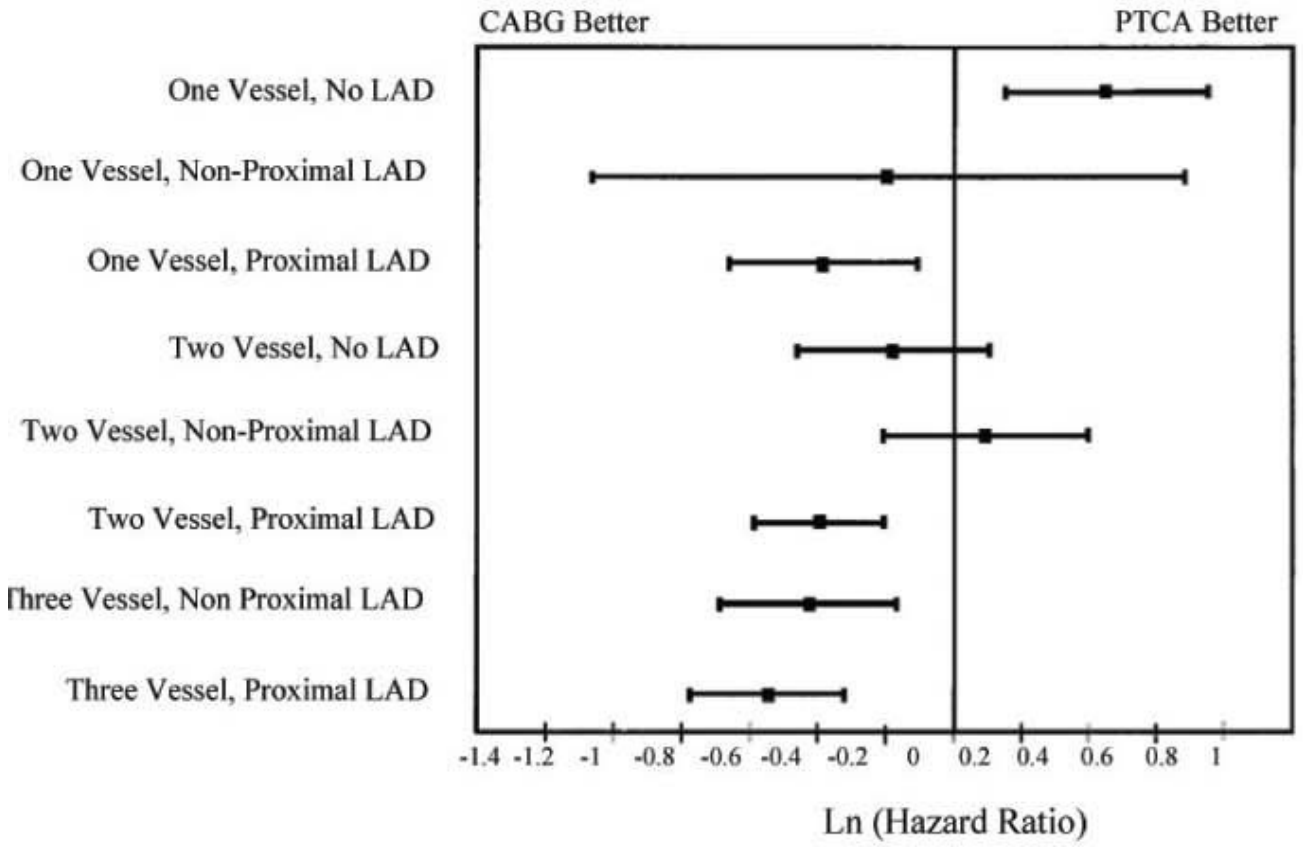
Current guidelines ACC/AHA 2004

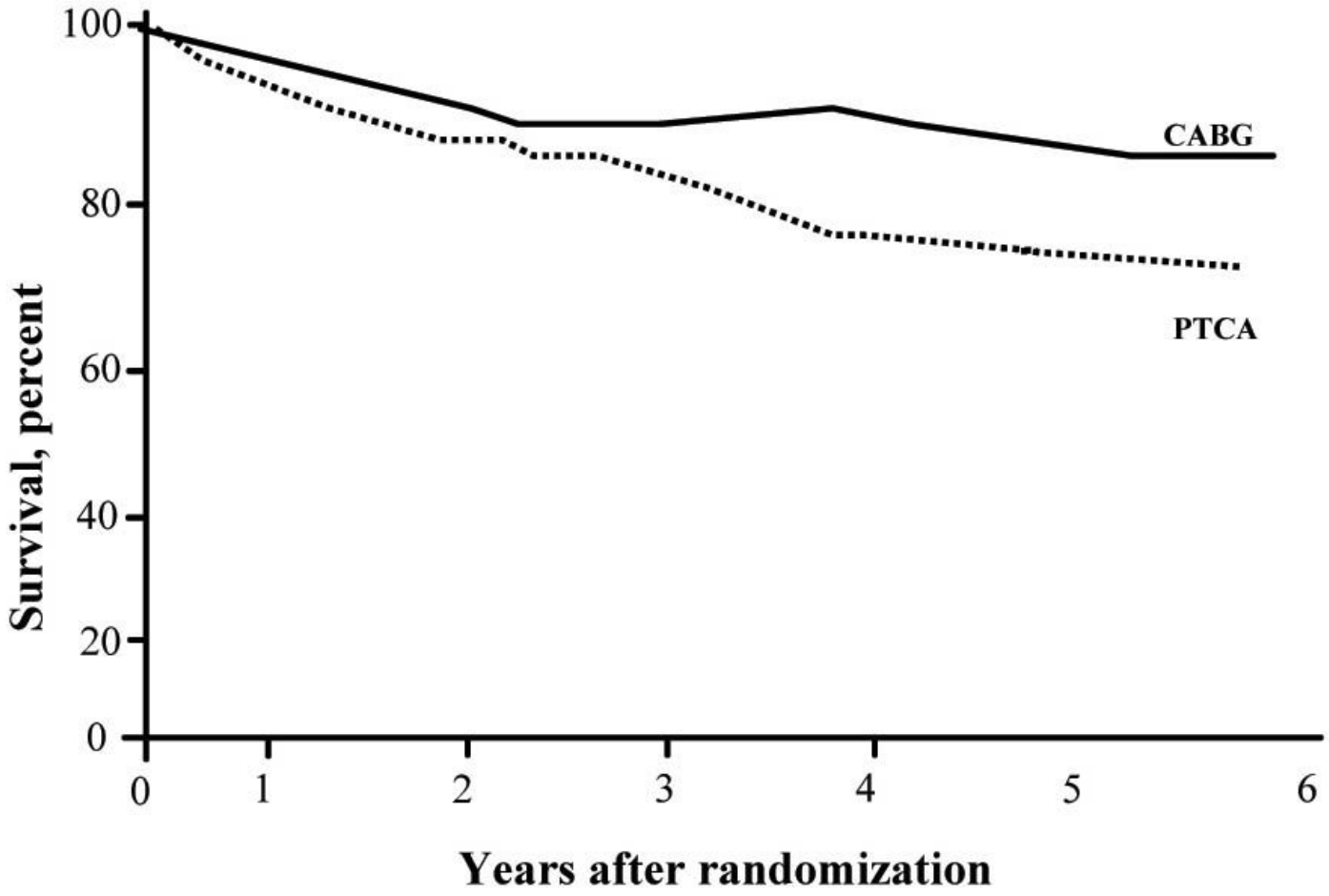
- **Asymptomatic/mild anginaClass** I
- Left main stenosis
- Left main equivalent (proximal LAD and proximal circumflex)
- Triple-vessel disease
- **Class IIa**
- Proximal LAD stenosis and one- or two-vessel disease
- **Class IIb**
- One- or two-vessel disease not involving proximal LAD
  If a large territory at risk on non invasive studies or LVEF < 50%, IIa and IIb become class I indications
- **Stable anginaClass I**
- Left main stenosis
- Left main equivalent (proximal LAD and proximal circumflex)
- Triple-vessel disease
- Two-vessel disease with proximal LAD stenosis and EF < 50% or demonstrable ischemia
- One- or two-vessel disease without proximal LAD stenosis but with a large territory at risk and high risk criteria on noninvasive testing
- **Disabling angina refractory to medical therapy**
- **Class IIa**
- proximal LAD stenosis with one vessel disease
- One- or two-vessel disease without proximal LAD stenosis, but with a moderate territory at risk and demonstrable ischemia
  If a large territory at risk on noninvasive studies and meets high risk criteria on noninvasive testing becomes a class I indication

Current guidelines ACC/AHA 2004

- **Unstable angina/non-ST-segment elevation MI (NSTEMI)Class I**
- Left main
- Left main equivalent
- Ongoing ischemia not responsive to maximal nonsurgical therapy
- **Class IIa**
- proximal LAD stenosis with one- or two-vessel disease
- **Class IIb**
- One- or two-vessel disease without proximal LAD stenosis when PCI not possible (becomes class I if high risk criteria on noninvasive testing)
- **ST-segment Elevation (Q-wave) MIClass I**
- Failed PCI with persistent pain or hemodynamic instability and anatomically feasible
- Persistent or recurrent ischemia refractory to medical treatment with acceptable anatomy who have a significant territory at risk and not a candidate for PCI
- Requires surgical repair of postinfarction ventricular septal rupture or mitral valve insufficiency
- Cardiogenic shock in patients less than 75 years of age who have ST-segment elevation, LBBB, or a posterior MI within 18 hours of onset
- Life-threatening ventricular arrhythmias in the presence of 50% left main stenosis or triple-vessel disease
- **Class IIa**
- Primary reperfusion in patients who have failed fibrinolytics or PCI and are in the early stages (6–12 hours) of an evolving STEMI
- Mortality with CABG is elevated the first 3–7 days after STEMI/NSTEMI. After 7 days, criteria for revascularization in previous sections apply

	Trial (Ref)	Age, y (% Female)	CAD	N	Acute Outcome% Death: CABG PCI	Acute Outcome% QW-MI:CABG PCI	Acute Outcome% Hosp CABG	Late Outcome, % Death	Late Outcome, % QW-MI	Late Outcome, % Angina	Late Outcome, % RR% Total/PCI/CABG	Primary End Point	Primary End Point, %	F/U, y
PTCA Trials	BARI	61 (26%)	MV	1829	1.3	4.6	N/A	15.6¶	19.6	N/A	8/7/1	D	15.6¶	8§
	(117)				1.1	2.1	6.3	19.1¶	21.3	N/A	54/34/31		19.1¶	
	EAST	61 (26%)	MV	392	1	10.3	N/A	17	19.6	12	13/13/1	D+MI+T	27.3	8‖
	(119)				1	3.0†	10.1	21	16.6	20†	54/41/22		28.8	
	GABI	N/A (20%)	MV	359	2.5	8	N/A	6.5	9.4	26	6/5/1	A	26	1
	(776)				1.1	2.3†	8.5	2.6	4.5	29	44/27/21		29	
	Toulouse	67 (23%)	MV	152	1.3	6.6	N/A	10.5	1.3	5.3	9/9/0	A	5.2	5
	(778)				1.3	3.9	3.9	13.2	5.3	21.1†	29/15/15		21.1†	
	RITA	57 (19%)	SV+	1011	1.2	2.4	N/A	3.6	5.2	21.5	4/3/1	D+MI	8.6	2.5‡
	(126)		MV*		0.8	3.5	4.5	3.1	6.7	31.3†	31/18/19		9.8	
	ERACI	58 (13%)	MV	127	4.6	6.2	N/A	4.7	7.8	3.2	6/3/3	D+MI+A+RR	23	3
	(132)				1.5	6.3	1.5	9.5	7.8	4.8	37/14/22		53†	
	MASS	56 (42%)	SV	142	1.4	1.4	N/A	N/A	N/A	2	0/0/0	D+MI+RR	3	3
	(122)		(LAD)		1.4	0	11	N/A	N/A	18	22/29/14		24†	
	Lausanne	56 (20%)	SV	134	0	0	N/A	1.5	1.5	5	3/3/0	D+MI+RR	7.6	2‡
	(134)		(LAD)		0	0	2.9	0	2.9	6	25/12/13		36.8†	
	CABRI	60 (22%)	MV	1054	1.3	N/A	N/A	2.7	3.5	10.1	9/6/1	D	2.7	1
	(143)				1.3	N/A	N/A	3.9	4.9	13.9†	36/21/18		3.9	
STENT Trials	SoS	61 (21%)	MV	988	N/A	N/A	N/A	2	8	21	6/4/1	RR	6	1
	(139)							5†	5	34†	21†/13/9		21†	
	ERACI II	62 (21%)	MV	450	N/A	N/A	N/A	8	6	8	5/0/0	D+MI+CVA+RR	19	1.6
	(780)							3†	3[b]	15†	17†/0/5		23	
	ARTS	61 (24%)	MV	1205	N/A	N/A	N/A	3	5	10	4/3/1	D+MI+CVA+RR	12	1
	(137)							3	6	21†	21†/16/7		26†	
	AWESOME	67 (N/A)	MV	454	N/A	N/A	N/A	N/A	N/A	N/A	N/A	D	21	3
	(140)												20	
	SIMA	59 (21%)	SV	121	N/A	N/A	N/A	4	4	5	0/0/0	D+MI+RR	7	2.4
	(141)							2	5	9	24†/13/6		31†	
	LEIPZIG	62 (25%)	SV	220	N/A	N/A	N/A	2	5	21	8/8/0	D+MI+RR	15	0.5
	(781)							0	3	38†	29/25/4		31†	


CABG Better
PTCA Better
One Vessel, No LAD
One Vessel, Non-Proximal LAD
One Vessel, Proximal LAD
Two Vessel, No LAD
Two Vessel, Non-Proximal LAD
Two Vessel, Proximal LAD
Three Vessel, Non Proximal LAD
Three Vessel, Proximal LAD
-1.4 -1.2 -1 -0.8 -0.6 -0.4 -0.2 0 0.2 0.4 0.6 0.8 1
Ln (Hazard Ratio)


100
80
60
40
20
0
Survival, percent
0
1
2
3
4
5
6
Years after randomization
CABG
PTCA

Limitations 1

- Although the prospective, randomized studies do provide objective data directly applicable to the specific patient subset represented in the study, extrapolation of the results to the more heterogeneous populations seen clinically can only be made if the implicit caveats are clearly understood. We must be mindful of the inescapable tradeoff between selection bias in registry studies and entry bias in randomized studies.

Limitations 2

- A second limitation of these studies is a consequence of the over-representation of patients at lowest risk of death in randomized trials; most are statistically underpowered with respect to survival analysis. For example, given current survival statistics, we would need approximately 2000 patients in each arm of a study to detect a 30% difference in mortality. The problem is compounded by the exclusion of the very patients for whom one would anticipate a survival advantage with adequate revascularization, such as those with depressed ventricular function.
- Randomized studies frequently employ softer endpoints such as angina or quality of life or create composites of qualitatively different endpoints, such as death, stroke, and myocardial infarction (MI). Meaningful analysis is further complicated by relatively short-term follow-up in most studies.

Limitations 3

- A third limitation is that significant improvements in each of these treatment strategies are occurring constantly. Examples include the use of antiplatelet agents, ACE inhibitors, lipid-lowering therapy, ITA grafts, and intravascular stents and the development of drug-eluting stents. These advances, along with aggressive secondary prevention after revascularization, have reduced the morbidity and mortality of CAD steadily in all patients, making differences in the hard endpoint of survival difficult to demonstrate.

Conclusion (ACC 2004-2005)

- In conclusion, the randomized trials of PCI versus CABG are useful, but only if results are interpreted in a context of patients entering or eligible to enter these trials.
- PCI is a reasonable alternative to CABG, and for many patients, it is the preferred initial approach, provided that the patient understands that there may be a higher incidence of recurrent angina and need for repeat revascularization procedures. This applies to patients with multivessel disease and preserved LV function in the main.
- For most patients similar to those included in these published trials, it is reassuring that a non-surgical revascularization procedure does not place them at increased risk of MI or death in comparison with the outcomes of surgical therapy. To extrapolate these results to patients who are not eligible for entry, however, it is intellectually flawed and potentially misleading.

Cochrane 2005

- Nine studies (3519 patients) were included.
- Participants were adults with stable angina or ACS and unstable angina and had either single or multiple vessel disease.
- Four RCTs included patients with multiple vessel disease, five focused on single vessel disease.
- Four studies reported beyond 1 year.
- No statistical differences were observed between CABG and stenting for meta-analysis of mortality or AMI, but there was heterogeneity.
- Composite cardiac event and revascularisation rates were lower for CABG than for stents.

Conclusion

- Considerably more data is needed to make firm long term conclusions on the implications for practice, but in the short to medium term, CABG has far less repeat revascularisation procedures than PTCA with stents currently in common clinical use.
- Future trials should recruit more realistic patient groupings, as the population selected for inclusion in the current review were prone to bias.
- selection tended to focus on patients with generally less co-morbidities and with better left ventricular function than the overall population presenting for revascularisation in the real world setting.

NEJM 2005

- We used New York's cardiac registries to identify 37,212 patients with multivessel disease who underwent CABG and 22,102 patients with multivessel disease who underwent PCI from January 1, 1997, to December 31, 2000
- The primary purpose of the data analyses was to determine whether long-term mortality differed significantly between patients undergoing CABG and those undergoing PCI, after controlling for differences in patients' preprocedural risk.
- A secondary purpose was to determine whether there were treatment-related differences in long-term mortality among patients with diabetes, patients with compromised ventricular function (defined by a left ventricular ejection fraction of less than 40 percent),and patients without compromised ventricular function.

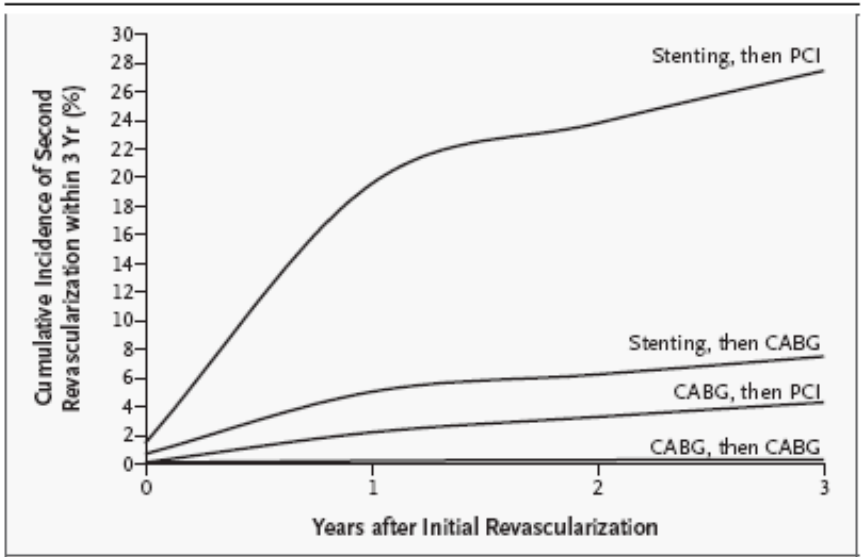
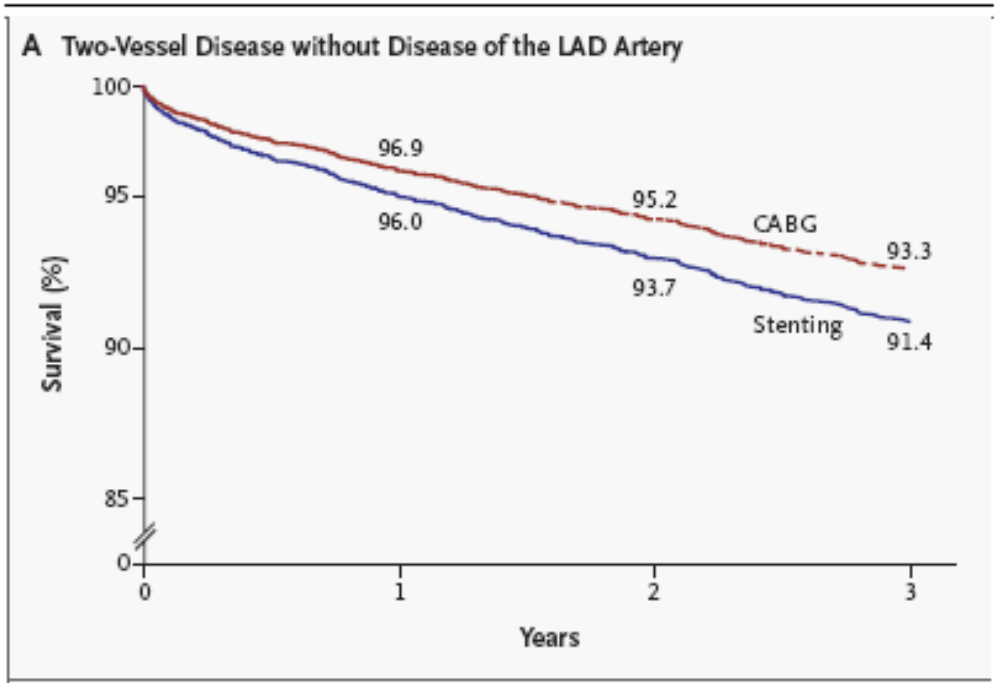
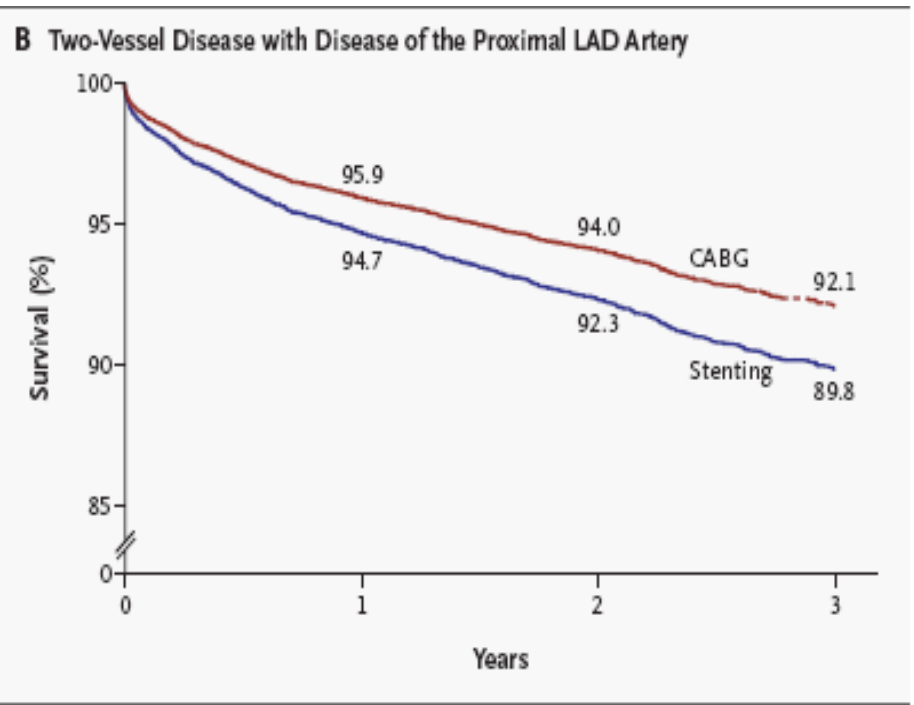
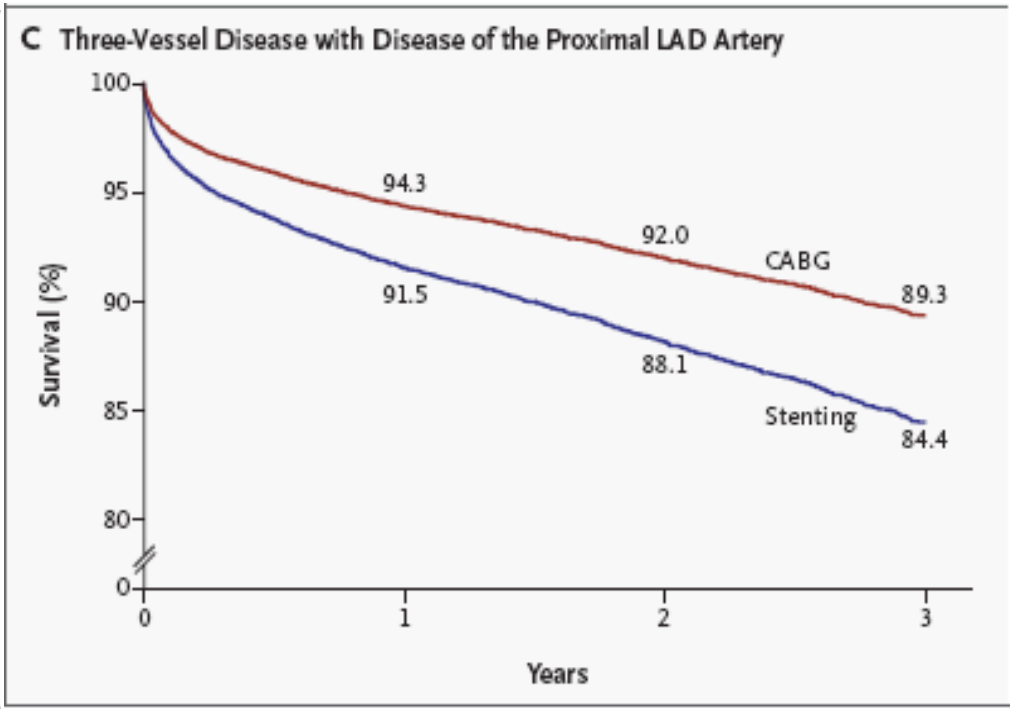


Figure 1. Percentage of Patients Undergoing a Second Revascularization Procedure within Three Years.





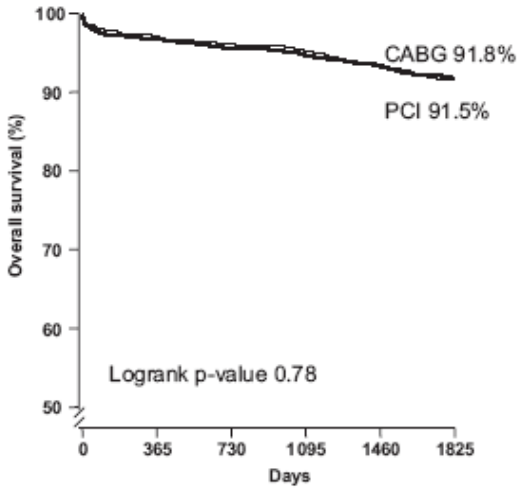


Limitations

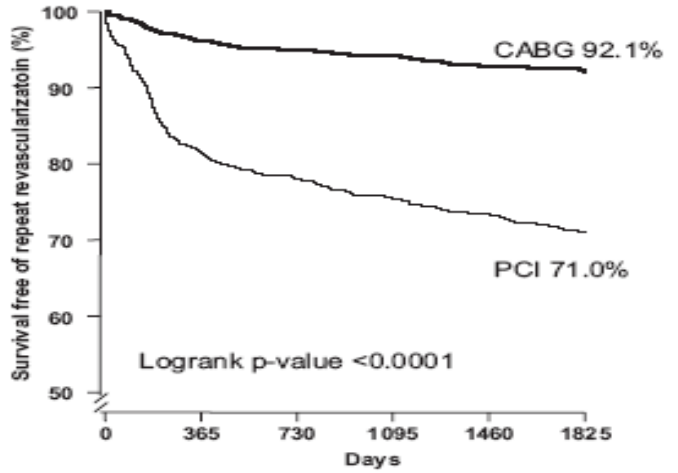
- Nevertheless, there remains the possibility that observational studies may fail to identify all confounders, and it is also true that propensity analyses cannot account for selection bias related to unmeasured characteristics.

Circulation Oct. 2008

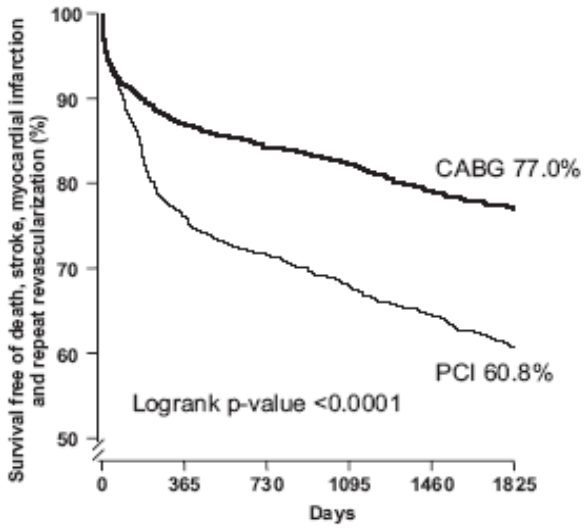
- A pooled analysis of 3051 patients in 4 randomized trials evaluating the relative safety and efficacy of PCI with stenting and CABG at 5 years for the treatment of multivessel coronary artery disease.
- The primary end point was the composite end point of death, stroke, or myocardial infarction.
- The secondary end point was the occurrence of major adverse cardiac and cerebrovascular accidents, death, stroke, myocardial infarction, andrepeat revascularization.



Group	0	365	730	1095	1460	1825
PCI	1518	1472	1456	1440	1406	1347
CABG	1533	1479	1457	1439	1412	1349



Group	0	365	730	1095	1460
PCI	1518	1204	772	740	707
CABG	1533	1428	927	911	882



Group	0	365	730	1095	1460	1825
PCI	1518	1153	729	691	657	616
CABG	1533	1332	867	846	812	785

Limitations

- However, patients with severe 3-vessel disease presenting with an acute coronary syndrome, left main lesions, previous coronary interventions, heart failure, or renal disease were excluded in all 4 trials.

Conclusion

- PCI was associated with a long-term safety profile, expressed by death, stroke, and MI, similar to that of CABG.
- However, because of the persistently lower repeat revascularization rates in the CABG patients, overall major adverse cardiac and cerebrovascular event rates were significantly lower in the CABG group at 5 years.
- Dedicated trial data on the impact of drug-eluting stents, the relief of angina, and the role of PCI in higher-risk patients are warranted.

Annals of Thoracic Surgery 2008

- A prospective registry of coronary revascularization by CABG on-pump and off pump, and PCI with or without DES, to determine clinical outcomes.
- *Methods.* All patients undergoing isolated coronary revascularization in 8 community-based hospitals were enrolled. Preprocedural, intraprocedural, and post procedural data were captured, with outcomes obtained at 18 months by patient and physician contact, and the Social Security Death Index.

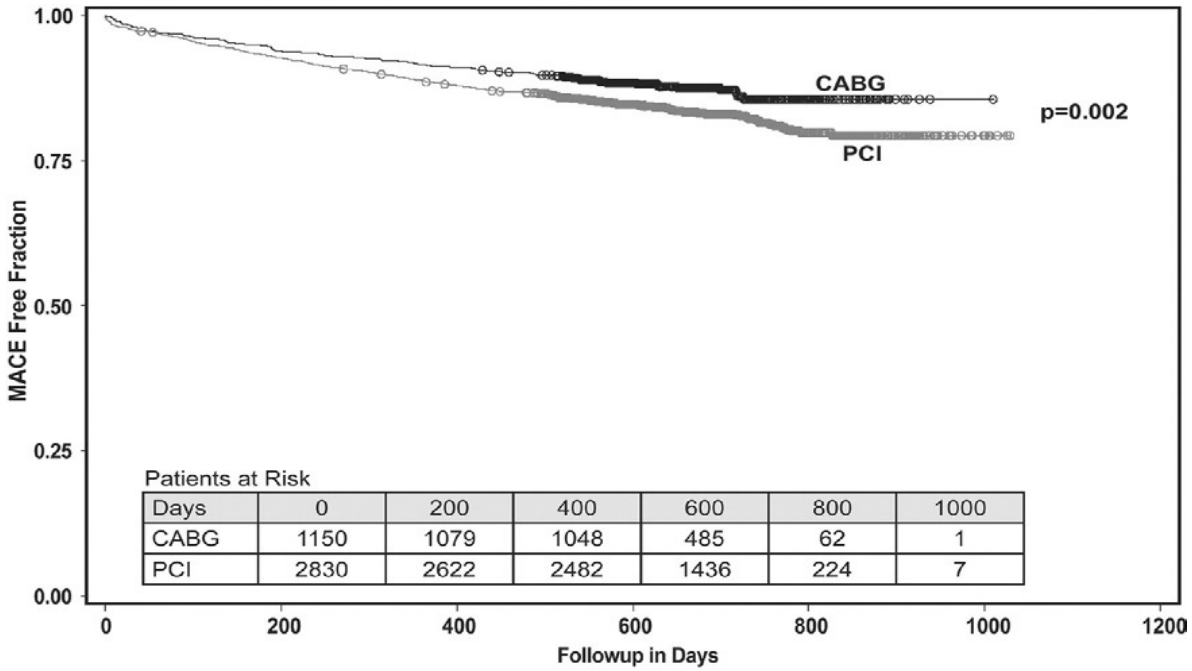


Table 2. Severity of Disease in Coronary Artery Bypass Graft and Percutaneous Coronary Intervention Patients

Diseased Vessel	CABG, %	PCI, %	*p* Value	Off-pump, %	On-pump, %	*p* Value
1-vessel	9.7	48.1		16.1	5.6	
2-vessel	30.5	32.3	< 0.001	34.7	27.8	< 0.001
3-vessel	59.8	19.6		49.2	66.6	

Conclusion

- We found no differences in any outcomes between on-pump and off-pump CABG.
- Patients who received DESs had less need for repeat revascularization than patients who received BMSs, but this was not statistically significant.
- We also found no mortality difference between CABG and PCI; however, this potential benefit of CABG has only been apparent in larger population studies with longer follow-up.

Limitations

- Despite the inclusion of more than 4000 patients in this study, it is still underpowered to detect any potential mortality benefit.
- Another limitation is the ability to achieve only 90%follow-up. The Sunbelt has a mobile population, and higher rates of follow-up were not achievable.
- The relatively short period of follow-up is also a limitation. An observation period of 18 months is still too short to detect differences in major outcomes, as has been seen in observational studies with large populations.
- We intend to obtain additional funding for continued follow-up for at least a 5-year period.

NEJM 2008

- Some 9963 patients receiving drug-eluting stents and 7437 patients undergoing CABG between October 1, 2003, and December 31, 2004, were followed through December 31, 2005, for myocardial infarction resulting in readmission, death, and repeat revascularization.
- The main purpose of the study was to compare differences in adverse outcomes between the two procedures.
- Another purpose, identified at the beginning of the study, was to compare adverse outcomes in subgroups of patients at high risk (patients with diabetes, patients 80 or more years of age, and patients with low left ventricular ejection fractions).

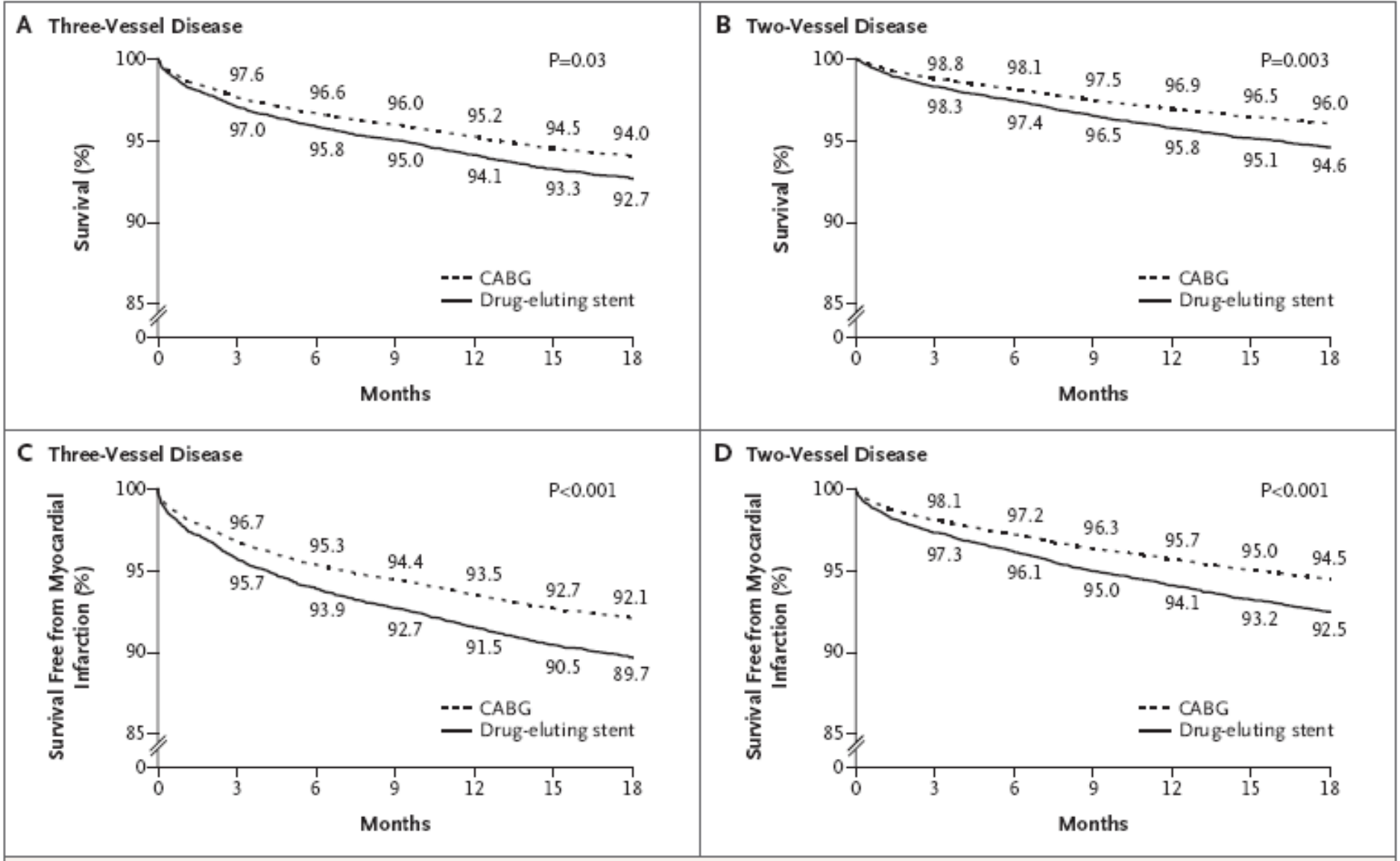


Figure 3. Adjusted Curves for Long-Term Survival and Survival Free from Myocardial Infarction According to the Number of Diseased Vessels.

Panels A through D show survival curves adjusted for age; sex; ejection fraction; hemodynamic state; history or no history of myocardial infarction before the procedure; the presence or absence of cerebrovascular disease, peripheral arterial disease, congestive heart failure, chronic obstructive pulmonary disease, diabetes, and renal failure; and involvement of the proximal left anterior descending (LAD) artery. CABG denotes coronary-artery bypass grafting.

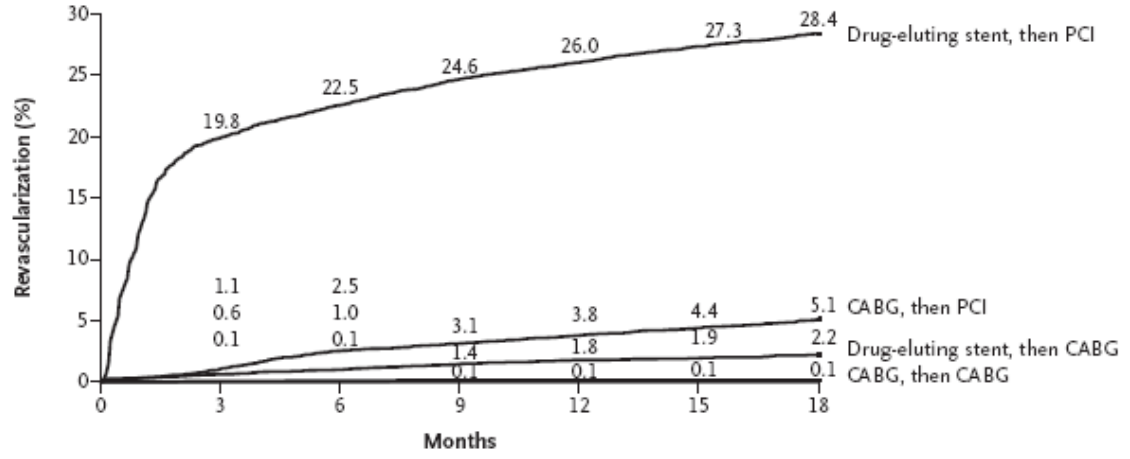


Figure 1. Rates of Revascularization within 18 Months after Initial Procedure.

CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

Conclusion

- Among patients with three-vessel disease or two-vessel disease, those treated with CABG had significantly lower adjusted rates of death and of death or myocardial infarction than those treated with drug-eluting stents;
- CABG was associated with lower rates of death or myocardial infarction for all subgroups of patients with multivessel disease defined by the presence or absence of proximal LAD artery disease
- In three high-risk subgroups of patients (patients with diabetes, patients with left ventricular ejection fractions below 40%, and patients 80 years of age or older), there were no significant differences in adjusted mortality rates between those undergoing CABG and those receiving drug-eluting stents, but patients with ejection fractions below 40% and patients who were at least 80 years old who underwent CABG had significantly lower rates of death or myocardial infarction.

Limitations

- Data on the severity of diabetes and insulin dependence were not available, and to the extent that one treatment (e.g., CABG) is associated with more severe diabetes, the risk-adjustment process was unable to control for those differences.
- Observational studies are subject to potential bias with respect to the relative preprocedural severity of illness among patients treated with CABG and drug-eluting stents.

	CABG (N=7437)	Stent (N=9963)	
No. of diseased vessels (%)‡			<0.001
3, with proximal LAD artery	51.5	11.8	
3, without proximal LAD artery	18.4	13.1	
2, with proximal LAD artery	20.0	26.1	
2, without proximal LAD artery	10.1	49.0	

Octogenarians Mayo clinic 2008

- A meta-analysis of 66 studies of coronary revascularization in patients aged over 80 years.
- The primary endpoints included 30 day mortality and long-term survival. Subgroup analyses stratified by revascularization type (PCI versus CABG) were also performed.

Table 1 Results of pooled estimates for 30 day mortality, short and long-term survival.

CABG and PCI studies	**Pooled estimate**	**95% CI**
30 Day mortality	6.3%	5.3–7.4
1 Year survival	86%	84–88
3 Year survival	78%	74–81
5 Year survival	67%	61–72
CABG studies		
30 Day mortality	7.2%	6.3–8.2
1 Year survival	86%	83–88
3 Year survival	78%	74–82
5 Year survival	68%	62–73
PCI studies		
30 Day mortality	5.4%	4.4–6.4
1 Year survival	87%	84–91
3 Year survival	78%	68–87
5 Year survival	62%	46–77

Octogenarians Annals 2007

- We identified 1693 patients, aged 80 to 89,with two-vessel disease (57.6%) or three-vessel disease (42.4%), without left main disease, undergoing a first, non emergency revascularization from 1992 to 2001.

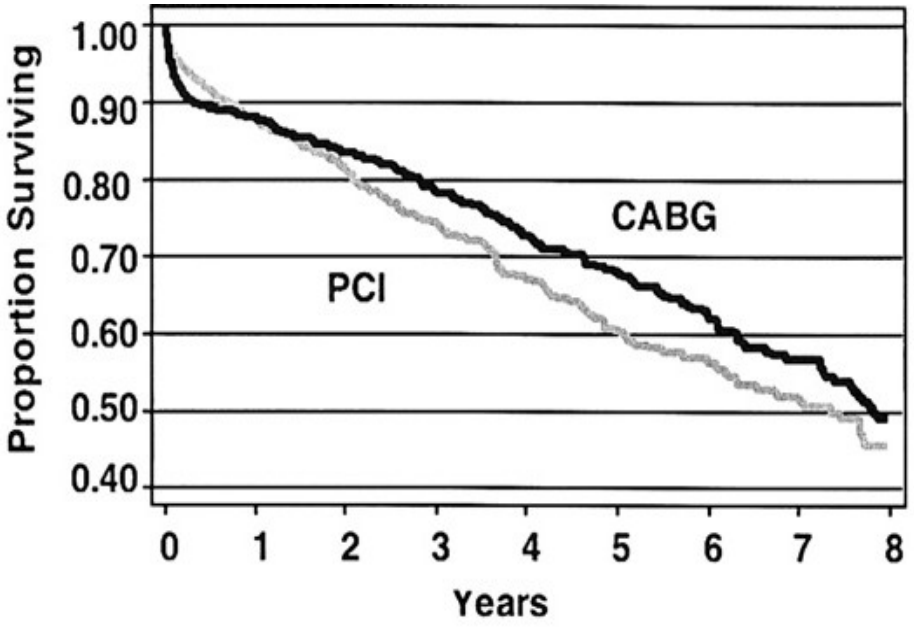


Fig 1. Kaplan-Meier survival curves of all patients undergoing percutaneous coronary intervention (PCI, gray line) and coronary artery bypass grafting (CABG, black line).

Conclusion

- Patients aged 80 years or older with multivessel disease must consider the trade-off between the increased early risks of CABG in return for improved long-term survival.

Costs - Effects

- The most recently published articles that included US-derived clinical outcomes and costs of revascularization were selected for review. Cost estimates were abstracted and updated to 2003.

Although initial estimated costs are lower for multivessel PCI (with or without stenting) than CABG, longer-term costs and lifetime costs are similar.

Table 2. Recent Cost Estimates of PCI Versus CABG in Multivessel Disease

Cost Category	PCI Population	Mean Cost ($) (2003)	CABG Population	Mean Cost ($) (2003)	Source (year)
Initial hospitalization	Multivessel stenting	13 454	CABG	23 438	Reynolds (2003)
	PTCA registry group	17 682	CABG registry group	36 877	Weintraub (2000)
	PTCA randomized group	25 105	CABG randomized group	31 732	Weintraub (2000)
Total 2 year	Multivessel stenting	20 088	CABG	27 669	Reynolds (2003)
Total 3 year	PTCA registry group	32 988	CABG registry group	59 588	Weintraub (2000)
	PTCA randomized group	50 400	CABG randomized group	55 553	Weintraub (2000)
Total 8 year	PTCA registry group	35 002	CABG registry group	59 869	Weintraub (2000)
	PTCA randomized group	56 343	CABG randomized group	58 948	Weintraub (2000)
Total lifetime	Initial angioplasty with provisional stenting	154 360	CABG with provisional stenting	154 018	Yock (2003)
	Initial angioplasty with primary stenting	163 587	CABG with primary stenting	159 258	Yock (2003)
			CABG without stenting	154 588	Yock (2003)

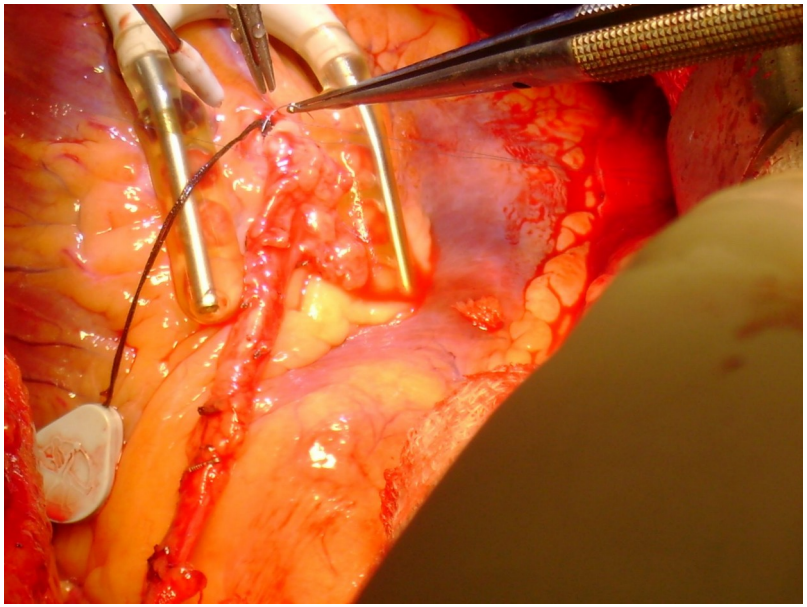
The studies providing the cost estimates had different designs and each cost estimate should be considered in the context of the clinical and cost studies from which it is derived.
Original costs from each source are updated to 2003 US dollars based on the Consumer Price Index-All Urban Consumers, Medical Care.
PCI indicates percutaneous coronary intervention; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty.

(Am J Manag Care. 2004;10:S370-S376)

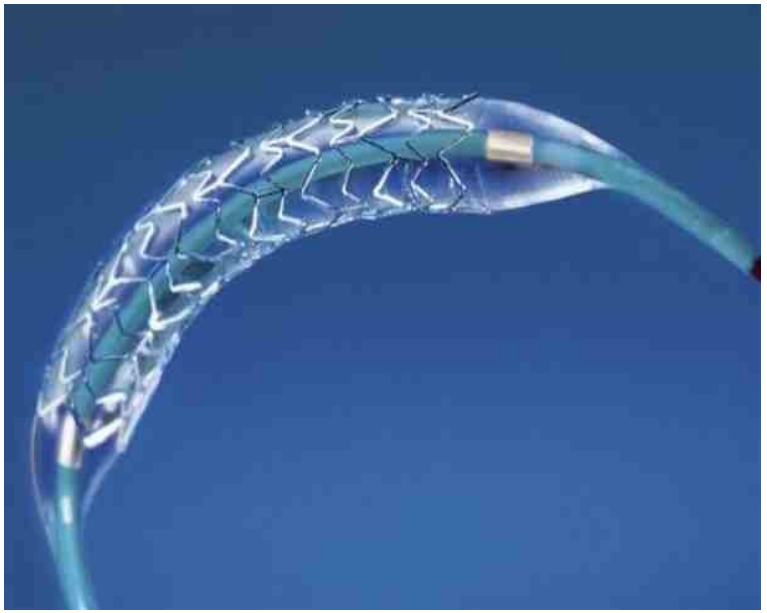
Summary

- CABG superior in LMS or equivalent and 2 or 3 vessel with high risk (impaired LV, ± diabetes) or proximal LAD involvement.
- PCI probably preferable for single vessel (not proximal LAD).
- Gray area of 2 vessel and 3 vessel with good LV where debate still continues.
- Ongoing CARDIA and FREEDOM trials to assess diabetes.
- Long term results of stents not available yet.

Questions, discussion



or



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