

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Seung KB, Park D-W, Kim Y-H, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med* 2008;358:1781-92. DOI: 10.1056/NEJMoa0801441.

**Supplementary Appendix for Seung et al., “Stents versus Coronary-Artery
Bypass Grafting for Left Main Coronary Artery Disease”**

I. Indications and Contraindications for Percutaneous Coronary Intervention (PCI)

II. Stent Implantation Methods

III. Methods of Propensity-Score Matching

IV. Outcomes of the Unmatched Patients

V. Acute Complications in PCI Patients and Angiographic Stent Thrombosis

I. Indications and Contraindications for PCI

In the centers participating in this study, PCI for unprotected left main disease is considered when patients have coronary anatomy suitable for stenting, have refused bypass surgery, or are at high risk for CABG. Although the inclusion criteria and strategy of PCI were determined by each center, the factors which were generally considered are listed in **Appendix Table 1**.

II. Stent Implantation Methods

Stent implantation methods for left main disease have been described previously.¹⁻⁴ Ostial or shaft lesions were attempted with a single stent placement. For bifurcation lesions, a single-stent technique, in which a stent was placed across the side branch (usually the left circumflex artery), was preferred in patients with diminutive or normal-appearing side branches. Two-stent techniques, which consisted of T-stenting, kissing stenting, culotte technique or crush technique, were considered in patients with diseased side branches. The use of predilation, intra-aortic balloon pump or intravascular ultrasound was at the discretion of the operator. Stent overexpansion with high-pressure inflation was performed in selected patients with suboptimal expansion or stent inapposition by angiography or intravascular ultrasound evaluation. Debulking devices including cutting balloon angioplasty, rotablator or debulking coronary atherectomy were used in selected patients with severe calcified or fibrous plaque at the operator's discretion.

III. Methods of Propensity-Score Matching

The propensity scores were estimated without regard to outcome variables, using multiple logistic-regression analysis.^{5,6} All prespecified covariates, which are listed in Table 1 of the article, were included in the final models for treatment with PCI versus CABG along with pertinent second-order interactions using step-wise selection procedures. A propensity score, indicating the predicted probability of receiving a specific treatment conditional on the observed covariates, was then calculated from the logistic equation for each patient. Also, for each concurrent comparison (Wave 1 and Wave 2), a separate propensity score for PCI versus CABG was generated using the same method for the overall cohort and was incorporated for each analysis (see the **Appendix Table 2**). The predictive ability of each propensity-score model was assessed by means of the C statistic (0.86 for the entire cohort, 0.88 for Wave 1, and 0.86 for Wave 2), indicating good discrimination between two treatments.

Using the Greedy 5→1 digit match algorithm,⁷ we created propensity-score-matched pairs without replacement (a 1:1 match). Specifically, we sought to match each patient with PCI to one with CABG who had a propensity score that was identical to 5 digits. If this could not be done, the algorithm then proceeded sequentially to the next highest digit match (a 4-, 3-, 2-, or 1-digit) on propensity score to make “next-best” matches, in a hierarchical sequence until no more matches could be made. If a subject who received PCI could not be matched to any subject who received CABG on the first digit of the propensity score, that subject with PCI was discarded from the matched analysis. Once a match was made, previous matches were not reconsidered before making the next match. After all of the propensity-scores-matches were performed, we assessed the balance in baseline covariates between the two intervention groups with the paired *t*-

test or the Wilcoxon signed rank test for continuous variables, and the McNemar's test or marginal homogeneity test for categorical variables. These results are shown in Table 2 of the article.

IV. Outcomes of the Unmatched Patients

Outcomes for the unmatched individuals remaining after propensity matching are shown in **Appendix Figures 1, 2, and 3.**

V. Acute Complications in PCI Patients and Angiographic Stent Thrombosis

Acute procedural complications in patients with unprotected left main coronary artery disease who underwent percutaneous coronary intervention are shown in **Appendix Table 3**.

During follow-up period, 6 patients (0.5%) had angiographic stent thrombosis: 1 (0.3%) in patients who received bare-metal stents and 5 (0.6%) in patients who received drug-eluting stents (2 [0.3%] in patients treated with sirolimus-eluting stents and 3 [1.7%] in patients treated with paclitaxel-eluting stents). Among patients treated with bare-metal stents, 1 patient had subacute stent thrombosis (13 days after the procedure). Of those treated with drug-eluting stents, 1 patient had acute stent thrombosis, 3 patients had subacute stent thrombosis (3 days, 5 days, and 22 days after the procedure), and 1 patient had late stent thrombosis (201 days after the procedure).

Appendix Table 1. Indications and Contraindications for Percutaneous Coronary Intervention for Patients with Unprotected Left Main Coronary Artery Disease.

Indications for PCI, in which PCI was favored	
Absolute	<ul style="list-style-type: none"> • Patient who refuses surgery
Relative	<ul style="list-style-type: none"> • Suitable coronary anatomy for stenting at the left main with preserved left ventricular function • Lesion restricted to the left main ostium or shaft • Isolated left main lesion • Bail-out procedure (eg. dissection at the left main during angiography or PCI) • Acute myocardial infarction at the left main, in which emergent revascularization is necessary • Cardiogenic shock due to left main stenosis, in which emergent revascularization is necessary • Age \geq 80 years • Serious co-morbid disease (eg. chronic lung disease, poor general performance status, etc) • Life expectancy of less than 1 year • Prior CABG • Coronary anatomy unsuitable for CABG (eg. poor distal vessel run-off)
Contraindications for PCI, in which CABG was favored	
Absolute	<ul style="list-style-type: none"> • Contraindication to antiplatelet therapy including aspirin, heparin, or thienopyridine (ticlopidine or clopidogrel) • History of serious allergic reaction to stainless steel, coated drug on stent, or contrast agent • History of known coagulopathy or bleeding diathesis • Pregnancy • Patient who refuses PCI
Relative	<ul style="list-style-type: none"> • Complex coronary anatomy at the left main, unsuitable for stenting (eg. severe calcification, severe tortuosity, etc)

	<ul style="list-style-type: none">• Total occlusions at other major epicardial coronary arteries (≥ 2)• Multiple and diffuse coronary stenosis, unsuitable for stent placement at the operator's discretion• Severely compromised left ventricular function• Extensive peripheral vascular disease, ineligible for placement of guiding catheter or intra-aortic balloon pump• In-stent restenosis at the left main, ineligible for repeat PCI
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Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery

Appendix Table 2. The Significant Covariates and Their Corresponding Weights in Each of the Propensity Score Models.

Overall Patients			Wave 1*			Wave 2*		
Variables	Beta Estimate	P value	Variables	Beta Estimate	P value	Variables	Beta Estimate	P value
Age (yr)	-0.08	0.008	Peripheral vascular disease	-2.17	0.005	Hypertension	0.32	0.008
Hypertension	0.22	0.03	Extent of diseased vessel		<0.001	Previous coronary angioplasty	0.71	<0.001
Previous coronary angioplasty	-1.82	0.04	Left main only	-†	-	Ejection fraction (%)	0.03	<0.001
Peripheral vascular disease	-1.02	0.001	Left main plus single-vessel disease	0.39	0.01	Clinical indication		<0.001
Ejection fraction (%)	0.02	<0.001	Left main plus double-vessel disease	-0.40	0.004	Silent ischemia	0.39	0.17
Clinical indication		<0.001	Left main plus triple-vessel disease	-1.15	<0.001	Chronic stable angina	0.02	0.88
Silent ischemia	0.19	0.40	Right coronary artery disease	-0.57	0.02	Unstable angina	-†	-
Chronic stable angina	0.18	0.10				NSTEMI	0.17	0.33
Unstable angina	-†	-				Extent of diseased vessel		<0.001
NSTEMI	0.10	0.48				Left main only	-†	-
Extent of diseased vessel		<0.001				Left main plus single-vessel disease	0.43	0.002
Left main only	-†	-				Left main plus double-vessel disease	-0.39	<0.001

Left main plus single-vessel disease	1.66	0.003	Left main plus triple-vessel disease	-0.88	<0.001
Left main plus double-vessel disease	-0.74	0.14	Right coronary artery disease	-0.67	<0.001
Left main plus triple-vessel disease	-2.59	<0.001			
Right coronary artery disease	-0.56	<0.001			
Age* Previous coronary angioplasty	0.04	0.003			
Age*Extent of diseased vessel		0.002			
Left main only	-†	-			
Left main plus single-vessel disease	-0.02	0.02			
Left main plus double-vessel disease	0.01	0.44			
Left main plus triple-vessel disease	0.03	0.001			

*Wave 1 shows comparisons between bare-metal stents versus concurrent bypass surgery and Wave 2 shows comparisons between drug-eluting stents versus concurrent bypass surgery.

†indicates reference category.

Appendix Table 3. Acute Complications in Patients with Unprotected Left Main Coronary Artery Disease who underwent Percutaneous Coronary Intervention.

Complications	Stenting (n=1102)
Acute vessel closure – n. (%)	2 (0.2)
Branch vessel occlusion – n. (%)	10 (0.9)
Coronary dissection – n. (%)	12 (1.1)
Coronary perforation – n. (%)	0
Emergency CABG – n. (%)	1 (0.1)
Death within 48 hours – n. (%)	9 (0.8)
Q-wave Myocardial infarction within 48 hours – n. (%)	2 (0.2)
Revascularization within 48 hours – n. (%)	2 (0.2)
Acute stent thrombosis (angiographic) – n. (%)	1 (0.1)
Overall – n. (%)	30 (2.7)

APPENDIX FIGURE LEGENDS

Appendix Figure 1. Kaplan-Meier Curves for Outcome in an Unmatched Cohort of Patients Who Underwent Stent Implantation or Bypass Surgery.

Propensity matching for the entire cohort created 542 matched pairs of patients. Outcomes for the remaining 1156 patients, who were not matched, are shown here. Panel A shows overall survival; Panel B shows freedom from death, Q-wave myocardial infarction (MI), or stroke; Panel C shows target-vessel revascularization (TVR). Event-free survival rates (at one, two, and three years) were derived from Kaplan-Meier curves. CABG denotes coronary-artery bypass grafting.

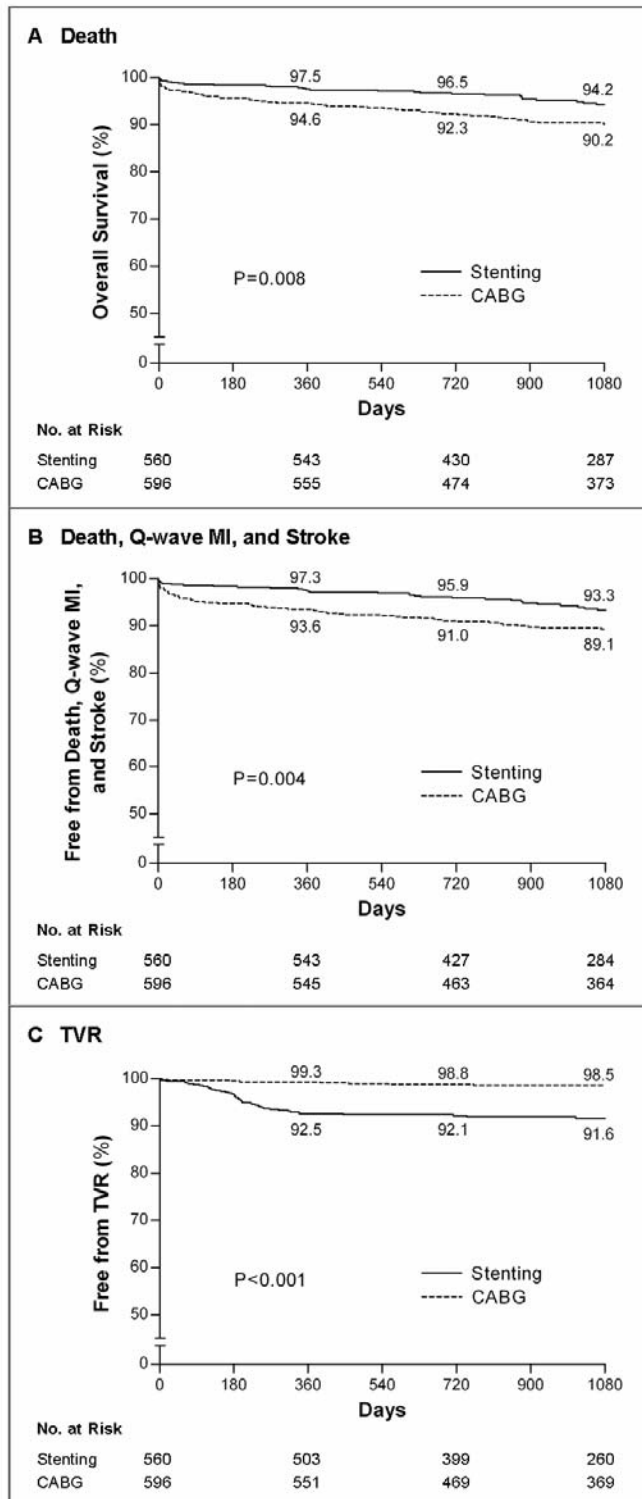
Appendix Figure 2. Kaplan-Meier Curves for Outcome in an Unmatched Cohort of Patients Who Underwent Stent Implantation with Bare-Metal Stents or Bypass Surgery.

Propensity matching for patients in Wave 1 created 207 matched pairs of patients. Outcomes for the remaining 352 patients, who were not matched, are shown here. Panel A shows overall survival; Panel B shows freedom from death, Q-wave myocardial infarction (MI), or stroke; Panel C shows target-vessel revascularization (TVR). Event-free survival rates (at one, two, and three years) were derived from Kaplan-Meier curves. CABG denotes coronary-artery bypass grafting.

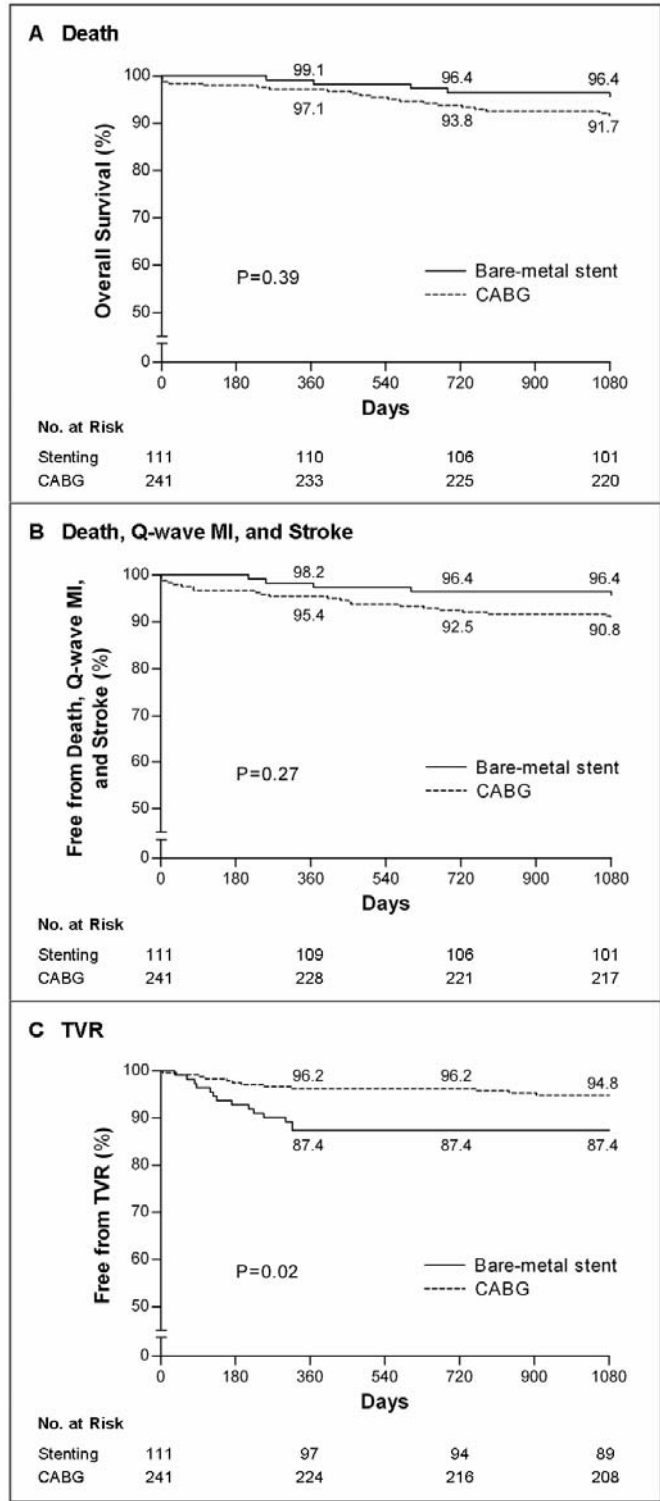
Appendix Figure 3. Kaplan-Meier Curves for Outcome in an Unmatched Cohort of Patients Who Underwent Stent Implantation with Drug-Eluting Stents or Bypass Surgery.

Propensity matching for patients in Wave 2 created 396 matched pairs of patients. Outcomes for the remaining 682 patients, who were not matched, are shown here. Panel A shows overall survival; Panel B shows freedom from death, Q-wave myocardial infarction (MI), or stroke; Panel C shows target-vessel revascularization (TVR). Event-free survival rates (at one, two, and three years) were derived from Kaplan-Meier curves. CABG denotes coronary-artery bypass grafting.

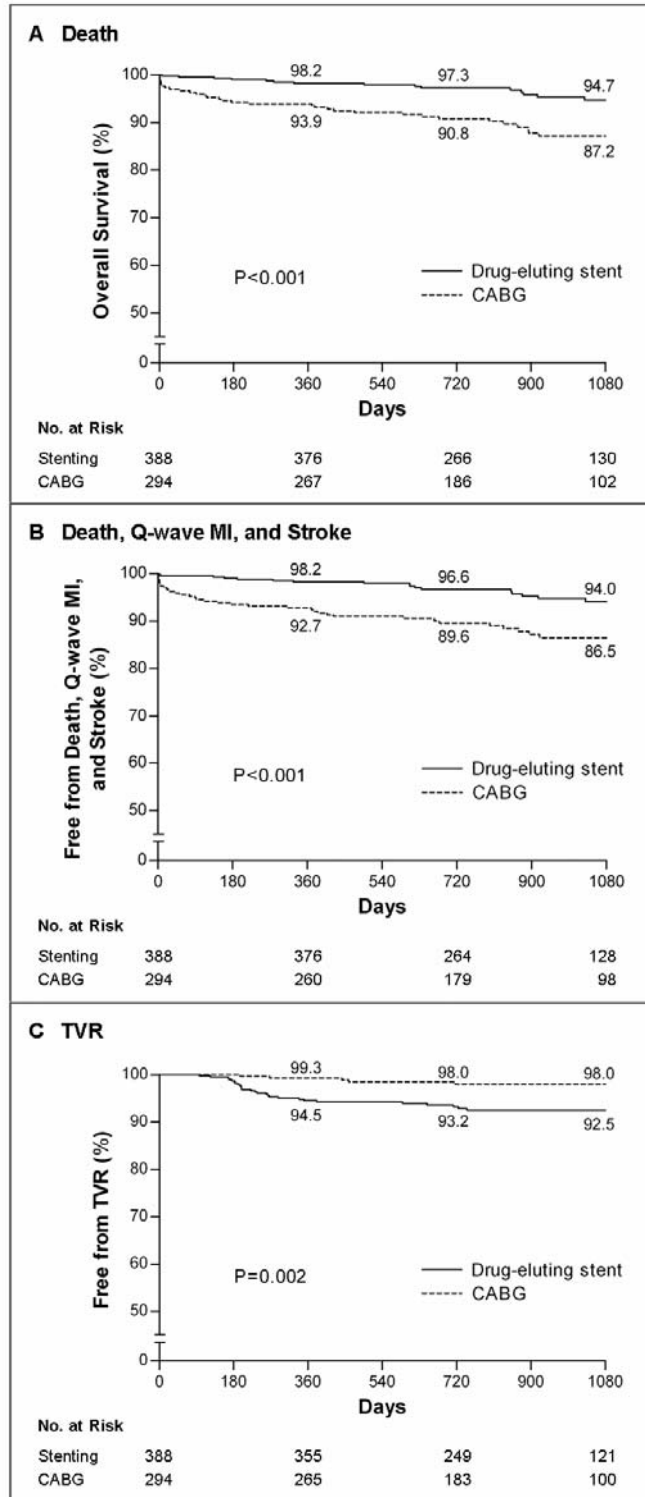
Appendix Figure 1.



Appendix Figure 2.



Appendix Figure 3.



References

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