Supplement to Stratification of Coronary Artery Disease Patients for Revascularization Procedure Based on Estimating Adverse Effects

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1 Patient Characteristics

Variable	Included	Excluded	P-value
Age	65.3 ± 10.3	68.9 ± 11.3	$5.23 \cdot 10^{-15}$
Female	405 (22.3%)	255 (27.9%)	$1.26 \cdot 10^{-3}$
Diabetic	418 (23.2%)	267 (29.5%)	$4.36 \cdot 10^{-4}$

Table S1: Comparison of patient characteristics of included and excluded interventions. From a total of 2,733 interventions, we excluded 913 interventions due to missing angiographic follow-up. Categorical variables were summarized by absolute counts and relative proportions and were compared with Fisher's exact test. Continuous variables were summarized by mean and standard deviation and compared using Welch's t-test.

2 Adverse Effects for Coronary Artery Bypass Grafting

Adverse effects of CABG treatment were retrieved from previously published randomized controlled trials. The probability of hazardous events (HE) was retrieved from eleven different trials shown in table S2. The definition of restenosis in the case of CABG is not straightforward, it could refer to reduced patency in the grafted vessel due to atherosclerosis or to a previously untreated lesion upstream of the original lesion. Here, we assumed the first definition and estimated $P(\text{Restenosis}|\text{CABG})$ to be 1.9% [4].

Study	Patients	Death	MI	Ref.
ARTS	603	17	28	[5]
ERACI II	225	16.875	14.175	[6]
AWESOME	232	48.72		[7]
SoS	500	4	34	[8]
MASS II	203	5	2	[9]
Myoprotect	21	5	0	[10]
Octostent	142	4	7	[11]
AMIST	47	1	0	[12]
Cisowski et al.	24	0	0	[13]
Kim et al.	50	4		[14]
SYNTAX	849	30	28	[15]
Hong et al.	68	0	5	[16]

Table S2: Randomized Control Studies used to estimate $P(\text{Hazard}|\text{CABG})$. Numbers indicate total number of patients with at least one occurrence of the specified clinical event up to one year after intervention. Decimal numbers occur when only percentage values were provided. MI indicates myocardial infarction.

3 Subgroups

Due to a smaller amount of data available for angiographic restenosis, a smaller number of subgroups was used, compared to the analyses considering clinical restenosis. Owing to insufficient data, our evaluation did not cover females younger than 60 years of age. In addition, for endpoints after 1 year, we could not factor in diabetics younger than 60 years old, and for angiographic restenosis we could not account for diabetic females older than 60 years of age. However, patients specific to these subgroups were part of supersets of these subgroups and therefore still included in the analyses, for instance females younger than 60 years are part of females of any age.

		1-yr HE		3-yr HE	
		BMS	DES	BMS	DES
Restenosis	Angiographic	133	157	133	185
	Clinical	148	157	148	185

Table S3: Number of subgroups generated for four different analyses. Bare-metal stent subgroups (BMS) were used to train classifiers to predict the probability of restenosis, and drug-eluting stent subgroups (DES) were used to predict hazardous events (HE).

Age	Gender	Diabetes
Age ≤ 60	*	Diabetic only
Age ≤ 60	Female	*
Age > 60	Female	Diabetic only

Table S4: Excluded subgroups due to insufficient data for prediction of hazardous events at 1 year. In total 10 subgroups were excluded. Asterisks indicate all three subgroups for this particular group, e.g. all genders, male and female.

Age	Gender	Diabetes
Age ≤ 60	*	Diabetic only
Age ≤ 60	Female	*

Table S5: Excluded subgroups due to insufficient data for prediction of angiographic and clinical restenosis, and 3-year hazardous events. In total 6 subgroups were excluded. Asterisks indicate all three subgroups for this particular group, e.g. all genders, male and female.

4 Costs

The costs were estimated based on Medicare reimbursements to hospitals in the U.S. for the year 2013[1]. Costs are based on full update national adjusted operating standardized amounts and capital standard federal rate averaged across all urban and rural areas. The base payment rate was $5,549.85. Costs for CABG were calculated by taking the weighted average of six different diagnosis-related groups (DRG) based on the number of cases in 2012: 231 (1.78%), 232 (1.54%), 233 (20.13%), 234 (32.19%), 235 (12.70%), and 236 (31.66%). Costs for BMS were calculated by the weighted average of DRG 248 (28.40%) and DRG 249 (71.60%). Accordingly, for DES where DRG 246 (21.74%) and DRG 247 (78.26%) were used. Costs for myocardial infarction are based on DRG 280 (46.78%), DRG 281 (32.39%), and DRG 282 (20.83%). Finally, for stroke we used DRG 61 (32.98%), DRG 62 (51.95%), and DRG 63 (15.06%). Corrective procedure costs where estimated by taking the weighted average of all DRGs comprising CABG, BMS, and DES from above. Following the current guidelines, we assumed one year of dual anti-platelet therapy for both BMS and DES and estimated the costs as $1 per day for generic clopidogrel [2, 3]. The final costs are in 2013 U.S. dollar are shown in table S6.

Variable	Costs in USD
C_{sBMS}	11,866.11
C_{sDES}	12,456.51
C_{sCABG}	28,683.40
$C_{\text{Corrective}}$	16,668.56
C_{MI}	7,537.75
C_{Stroke}	12,169.54
C_{DAPT}	365

Table S6: Costs in 2013 U.S. dollars assigned to individual treatments.

5 Analysis without Partitioning

	1-year Hazardous Events		3-year Hazardous Events	
	Mean	95% CI	Mean	95% CI
$\hat{P}$(sBMS)	2.3	1.8 – 9.1	3.1	1.8 – 9.1
$\hat{P}$(sDES)	90.5	84.8 – 92.0	89.1	83.3 – 90.5
$\hat{P}$(sCABG)	6.5	5.7 – 7.0	7.9	7.1 – 8.2
$\hat{P}$(Restenosis|sBMS)	0.0	0.0 – 0.0	0.0	0.0 – 0.0
$\tilde{P}$(Restenosis|sDES)	6.6	6.2 – 6.8	6.9	6.7 – 7.2
$\hat{P}$(Restenosis)	6.2	5.5 – 6.4	6.3	5.8 – 6.7
$\tilde{P}$(Hazard|sBMS)	0.2	0.0 – 0.0	4.5	0.0 – 33.3
$\hat{P}$(Hazard|sDES)	4.4	3.6 – 5.6	9.7	7.4 – 10.2
$\hat{P}$(Hazard)	4.5	3.6 – 5.6	9.5	7.4 – 11.7
Baseline P(Adverse Effect)	12.3	11.2 – 13.4	18.6	17.4 – 18.8
Proposed P(Adverse Effect)	10.6	9.1 – 12.0	15.8	14.3 – 17.7
ΔP(Adverse Effect)	1.7	1.4 – 2.6	2.8	0.9 – 3.8
Relative Risk Reduction (%)	13.8	10.2 – 20.1	15.1	4.7 – 20.5
Estimated Costs				
Initial Costs (Baseline)	13,795	13,749 – 13,847	13,822	13,782 – 13,852
Initial Costs (Proposed)	13,829	13,674 – 13,923	14,052	13,897 – 14,116
Corrective procedure (Baseline)	2,650	2,380 – 2,910	4,297	3,871 – 4,347
Corrective procedure (Proposed)	2,221	1,858 – 2,560	3,579	3,101 – 4,094
Total Savings	395	242 – 742	487	132 – 768
Total Savings (%)	2.4	1.5 – 4.4	2.7	0.7 – 4.2

Table S7: Estimated probabilities of adverse effects for angiographic restenosis and 1-year and 3-year hazardous events analysis, respectively, without constructing subgroup-specific classifiers. Baseline refers to treatment exclusively with drug-eluting stents and costs are in 2013 U.S. dollar.

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