Systemic Risk Stratification in Revascularization Therapy in Unprotected Left Main Coronary Stenosis LM-Risk Score

Young-Hak Kim, MD, PhD

Department of Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Usefulness of Risk Scoring System

- To predict outcomes of patients
- To select a appropriate treatment strategy for each patient
- To predict a need of adjunctive resources
- To compare outcomes of revascularization treatment in different hospitals and populations



Component of Euro SCORE

Risk factors	Score	Risk factors	Score
Cardiac-related factors		Patient-related factors	1
Unstable angina	2	Age	1
Left ventricular dysfunction	1	Sex	1
Left ventricular dysfunction	3	Chronic pulmonary disease	2
Recent myocardial infarction	2	Extracardiac arteriopathy	2
Pulmonary hypertension	2	Neurologic dysfunction	3
Operation-related factors		Previous cardiac surgery	2
Emergent operation	2	Serum creatinine	3
Other than isolated CABG	2	Active endocarditis	3
Surgery on thoracic aorta	3	Critical preoperative state	
Postinfarct septal rupture	4		



LM-Risk Score







Development of LM Risk Score Investigator Group

- Seung-Jung Park, MD
- Seong-Wook Park, MD
- Myeong-Ki Hong, MD
- Cheol-Whan Lee, MD
- Young-Hak Kim, MD
- Duk-Woo Park, MD

Asan Medical Center, CardioVascular Research Foundation, Seoul

- Martin B. Leon, MD
- Roxana Mehran, MD
- Ajay K. Kirtane, MD
- Helen Parise, ScD

Columbia University, Cardiovascular Research Foundation, NY

• Stuart J. Pocock, PhD

London School of Hygiene and Tropical Medicine, London

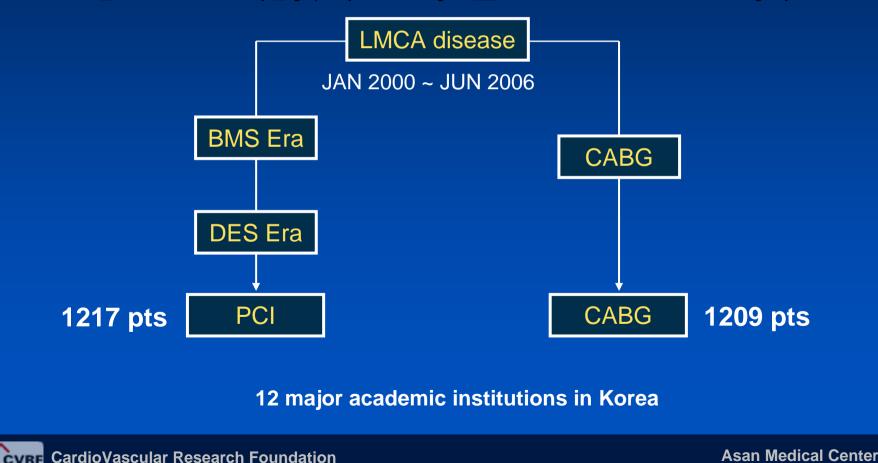




Discrimination of Risk Factors Population at Risk

2426 Patients in MAIN-COMPARE Registry

Revascularization for Unprotected Left <u>MAIN</u> Coronary Artery Stenosis: <u>COM</u>parison of <u>P</u>ercutaneous Coronary <u>A</u>ngioplasty versus Surgical <u>RE</u>vascularization from Multi-Center Registry





Statistical Analysis

- A multivariable Cox model was used to assess the statistical significance of each candidate prognostic variable.
- After each factor was tested independently in a univariate Cox model, those that achieved a significance level with p<0.05 were selected for testing in a multivariate stepwise selection.
- Variables associated with p<0.05 were retained in the final model and were used in developing risk score.
- Interaction test was performed according to the procedure types.
- The ROC curves were used to test the accuracy of the risk score.



Outcomes of Interest Death or Q-MI at 2 Years

	PCI (N=1217)	CABG (N=1209)	Total (N=2426)
F/U duration (days) Median [IQR]	707.00 [399.00, 1121.00]	909.00 [478.50, 1501.50]	797.50 [438.00, 1313.00]
Binary Outcomes			
Death	6.7%	7.4%	7.0%
Q-wave MI	0.6%	0.8%	0.7%
Death/Q-MI	6.9%	7.8%	7.3%
K-M Estimates			
Death	7.9%	8.1%	8.0%
Q-wave MI	0.6%	0.9%	0.7%
Death/Q-MI	8.0%	8.5%	8.2%



Candidate Predictors of Death/MI 37 Variables

DES (vs. BMS)	Smoking
Age	Chronic lung disease
Obesity (BMI > 30)	Significant valve disease
Female	Acute coronary syndrome
Previous PCI	Myocardial infarction
Previous MI	Atrial fibrillation
Previous CHF	TIMI flow
Diabetes mellitus	LV EF (%)
Hypertension	Cardiogenic shock
Hyperlipidemia	Indication of procedure
Previous CVA	Multivessel disease
Chronic renal failure	Extra-LM vascular involvement
Peripheral vascular disease	

RCA disease Lesion location Bifurcation type ACC/AHA type In-stent restenosis Infarct-related artery **Restenotic lesions** Lesion length **Total occlusion** calcification Thrombus Ulceration



Multivariate Cox Analysis PCI Groups

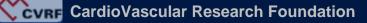
Multivariate Predictors	Coeff	SE	p value	Hazard Ratio [95% C.I.]	Risk Score
DES					
Age \geq 75	1.060	0.245	0.000	2.89 [1.79, 4.66]	4
Previous MI					
Hyperlipidemia					
Chronic renal failure	2.015	0.291	0.000	7.50 [4.24, 13.28]	7
Significant valve disease					
STEMI					
Atrial fibrillation	1.354	0.356	0.000	3.87 [1.93, 7.78]	4
Infarction Related	0.844	0.240	0.000	2.33 [1.45, 3.72]	4
EF, 30%-40%	0.915	0.336	0.007	2.50 [1.29, 4.83]	3
EF, <30%	1.824	0.416	0.000	6.20 [2.74, 14.03]	4
Emergent procedure					
RCA disease					
MEDINA 1.1.1 or 1.1.0					
Thrombus					



Multivariate Cox Analysis CABG Groups

Coeff	SE	p value	Hazard Ratio [95% C.I.]	Risk Score
0.861	0.254	0.001	2.36 [1.44, 3.89]	3
-0.644	0.264	0.015	0.53 [0.31, 0.88]	-2
0.857	0.359	0.017	2.36 [1.17, 4.76]	2
1.262	0.384	0.001	3.53 [1.66, 7.50]	3
1.519	0.360	0.000	4.57 [2.25, 9.28]	4
0.680	0.281	0.015	1.97 [1.14, 3.42]	2
0.625	0.222	0.005	1.87 [1.21, 2.89]	3
	0.861 -0.644 0.857 1.262 1.519 0.680	0.8610.254-0.6440.2640.8570.3591.2620.3841.5190.3600.6800.281	CoeffSEvalue0.8610.2540.001-0.6440.2640.0150.8570.3590.0171.2620.3840.0011.5190.3600.0000.6800.2810.015	CoeffSEvalue[95% C.I.]0.8610.2540.0012.36 [1.44, 3.89]-0.6440.2640.0150.53 [0.31, 0.88]0.8570.3590.0172.36 [1.17, 4.76]1.2620.3840.0013.53 [1.66, 7.50]1.5190.3600.0004.57 [2.25, 9.28]0.6800.2810.0151.97 [1.14, 3.42]

Thrombus





Multivariate Cox Analysis Combined Groups

Coeff	SE	p value	Hazard Ratio [95% C.I.]	Risk Score
0.966	0.169	0.000	2.63 [1.89, 3.66]	6
1.310	0.231	0.000	3.71 [2.36, 5.83]	6
0.645	0.255	0.011	1.91 [1.16, 3.14]	3
1.130	0.262	0.000	3.10 [1.85, 5.17]	4
0.458	0.189	0.016	1.58 [1.09, 2.29]	2
0.630	0.237	0.008	1.88 [1.18, 2.99]	3
1.667	0.261	0.000	5.30 [3.17, 8.84]	6
0.442	0.164	0.007	1.56 [1.13, 2.14]	3
0.756	0.294	0.010	2.13 [1.20, 3.79]	3
	0.966 1.310 0.645 1.130 0.458 0.630 1.667 0.442	0.9660.1691.3100.2310.6450.2551.1300.2620.4580.1890.6300.2371.6670.2610.4420.164	CoerrSEvalue0.9660.1690.0001.3100.2310.0000.6450.2550.0111.1300.2620.0000.4580.1890.0160.6300.2370.0081.6670.2610.0000.4420.1640.007	CoeffSEvalue[95% C.I.]0.9660.1690.0002.63 [1.89, 3.66]1.3100.2310.0003.71 [2.36, 5.83]0.6450.2550.0111.91 [1.16, 3.14]1.1300.2620.0003.10 [1.85, 5.17]0.4580.1890.0161.58 [1.09, 2.29]0.6300.2370.0081.88 [1.18, 2.99]1.6670.2610.0005.30 [3.17, 8.84]0.4420.1640.0071.56 [1.13, 2.14]





Multivariate Interaction Model Combined Group

Multivariate Predictors	Coefficient	SE	p value	Hazard Ratio [95% C.I.]	Risk Score
DES	-0.4410	0.2857	0.1227	0.64 [0.37, 1.13]	0
PCI	0.0674	0.3138	0.8299	1.07 [0.58, 1.98]	0
65 <= Age < 75	0.3190	0.1839	0.0828	1.38 [0.96, 1.97]	2
Age >= 75	1.0866	0.1971	0.0000	2.96 [2.01, 4.36]	6
EF <30%	1.7152	0.2656	0.0000	5.56 [3.30, 9.36]	7
STEMI	0.7855	0.2235	0.0004	2.19 [1.42, 3.40]	4



Multivariate Interaction Model Interaction Terms

Multivariate Predictors	Coeffi.	SE	p value	Hazard Ratio [95% C.I.]	Risk Score
Only add if CABG					
MEDINA 1.1.1 or 1.1.0 (ostial LAD involvement)	0.6383	0.2202	0.0038	1.89 [1.23, 2.92]	3
Only add if any PCI					
Chronic renal failure	1.7885	0.2831	0.0000	5.98 [3.43, 10.42]	6
Infarction Related	0.6735	0.2365	0.0044	1.96 [1.23, 3.12]	3
Only add if PCI with DES					
Significant valve disease	1.1136	0.5492	0.0427	3.05 [1.04, 8.94]	2
Low EF (30%-40%)	1.2647	0.3833	0.0010	3.54 [1.67, 7.51]	3
Total Occlusion	1.2899	0.4208	0.0022	3.63 [1.59, 8.29]	3
Only add if PCI with BMS					
Hyperlipidemia	-0.6378	0.2420	0.0084	0.53 [0.33, 0.85]	-3
Atrial fibrillation	1.4030	0.2910	0.0000	4.07 [2.30, 7.19]	5
RCA disease	0.5285	0.2344	0.0241	1.70 [1.07, 2.69]	2



Range of Scores





Asan Medical Center



Incidence of Observed Events (Death/Q-MI) According to the Risk Score

Risk Group	Total N	Non-	events	Events (D	eath/Q-MI)
Complete group (N=1604)		Ν	%	Ν	%
0 (Very Low)	613	601	98.04	12	1.96
1-5 (Low)	792	744	93.94	48	6.06
6-9 (Moderate)	255	220	86.27	35	13.73
≥ 10 (High)	69	39	56.52	30	43.48
Partial group (N=2248)					
0 (Very Low)	910	887	97.47	23	2.53
1-5 (Low)	1064	1003	94.27	61	5.73
6-9 (Moderate)	361	309	85.60	52	14.40
≥ 10 (High)	91	49	53.85	42	46.15

"Complete" refers to only patients who have non-missing data for ALL covariates.

"Partial" refers to all patients where all available data is used for the risk score. If a patient is missing data for a binary variable it is assumed that the patient does not have that risk factor (i.e. it is not added).



Incidence of Observed Events (Death/Q-MI) According to the Risk Score

		PCI	CA	BG
Complete group (N=1604)	Ν	%	N	%
0 (Very Low)	23	2.09	4	1.74
1-5 (Low)	13	4.00	35	7.49
6-9 (Moderate)	10	7.14	25	21.74
≥ 10 (High)	25	43.86	5	41.67
Partial group (N=2248)				
0 (Very Low)	9	1.75	14	3.53
1-5 (Low)	19	4.42	42	6.62
6-9 (Moderate)	19	9.74	33	19.88
≥ 10 (High)	37	46.84	5	41.67



Under the ROC Curve for 100 randomly selected samples

	Mean	SD	Median	IQR
Complete				
	0.6173	0.0263	0.6173	0.6003 – 0.6323
Partial				0 7400
	0.7262	0.0213	0.7259	0.7132 – 0.7403



Asan Medical Center



Example 69 Y Male, EF 42%, CRF, SA, LM extended to LAD, PCI with DES

	Patients	Risk Score	Patient risk
Overall			
DES	Yes	0	0
PCI	Yes	0	0
65 <= Age < 75	Yes	2	2
Age >= 75	No	6	0
EF < 30%	No	7	0
STEMI	Νο	4	0
Any PCI			
CRF	Yes	6	6
Infarct related	No	3	0
DES only			
Significant valve disease	No	2	0
EF 30-40%	No	3	0
Total occlusion	Νο	3	
Total score			8



Incidence of Expected Events (Death/Q-MI)

Complete group (N=1604)	PCI		CABG	
	Ν	%	Ν	%
0 (Very Low)	23	2.09	4	1.74
1-5 (Low)	13	4.00	35	7.49
6-9 (Moderate)	10	7.14	25	21.74
≥ 10 (High)	25	43.86	5	41.67
Partial group (N=2248)				
0 (Very Low)	9	1.75	14	3.53
1-5 (Low)	19	4 42	42	6.62
6-9 (Moderate)	19	9.74	33	19.88
≥ 10 (High)	37	46.84	5	41.67



Example 69 Y Male, EF 42%, CRF, SA, LM extended to LAD, CABG

	Patients	Risk Score	Patient risk
Overall			
DES	Yes	0	0
PCI	Yes	0	0
65 <= Age < 75	Yes	2	2
Age >= 75	No	6	0
EF < 30%	No	7	0
STEMI	No	4	0
CABG			
MEDINA 1.1.1 or 1.0.1 (ostial LAD involvement)	Yes	6	6
Total score			8





Incidence of Expected Events (Death/Q-MI)

Complete group (N=1604)	PCI		CABG	
	N	%	Ν	%
0 (Very Low)	23	2.09	4	1.74
1-5 (Low)	13	4.00	35	7.49
6-9 (Moderate)	10	7.14	25	21.74
≥ 10 (High)	25	43.86	5	41.67
Partial group (N=2248)				
0 (Very Low)	9	1.75	14	3.53
1-5 (Low)	19	4.42	42	6 62
6-9 (Moderate)	19	9.74	33	19.88
≥ 10 (High)	37	46.84	5	41.67



69 Y Male, EF 42%, CRF, Stable Angina, LM extended to LAD

We may recommend PCI with DES

Expected risk of Death/QMI in PCI with DES 7-10%
Expected risk of Death/QMI in CABG 20-22%



Asan Medical Center



Final Step External Validation

We need your help to get a large database...





Summary

- With the MAIN-COMPARE registry, the risk stratification system, so called "LM-Score", is being developed to provide a more accurate and reliable prediction of outcomes for patients with unprotected LMCA stenosis receiving revascularization therapy.
- In the preliminary analysis, the risk score appears to be effective to predict the outcomes of patients treated with either PCI or CABG.
- The predictability of final statistical model will be additionally ascertained by the process of external validation using a separated large database.

