Combination of Angiographic and Clinical Risk Scores in Left Main Revascularization

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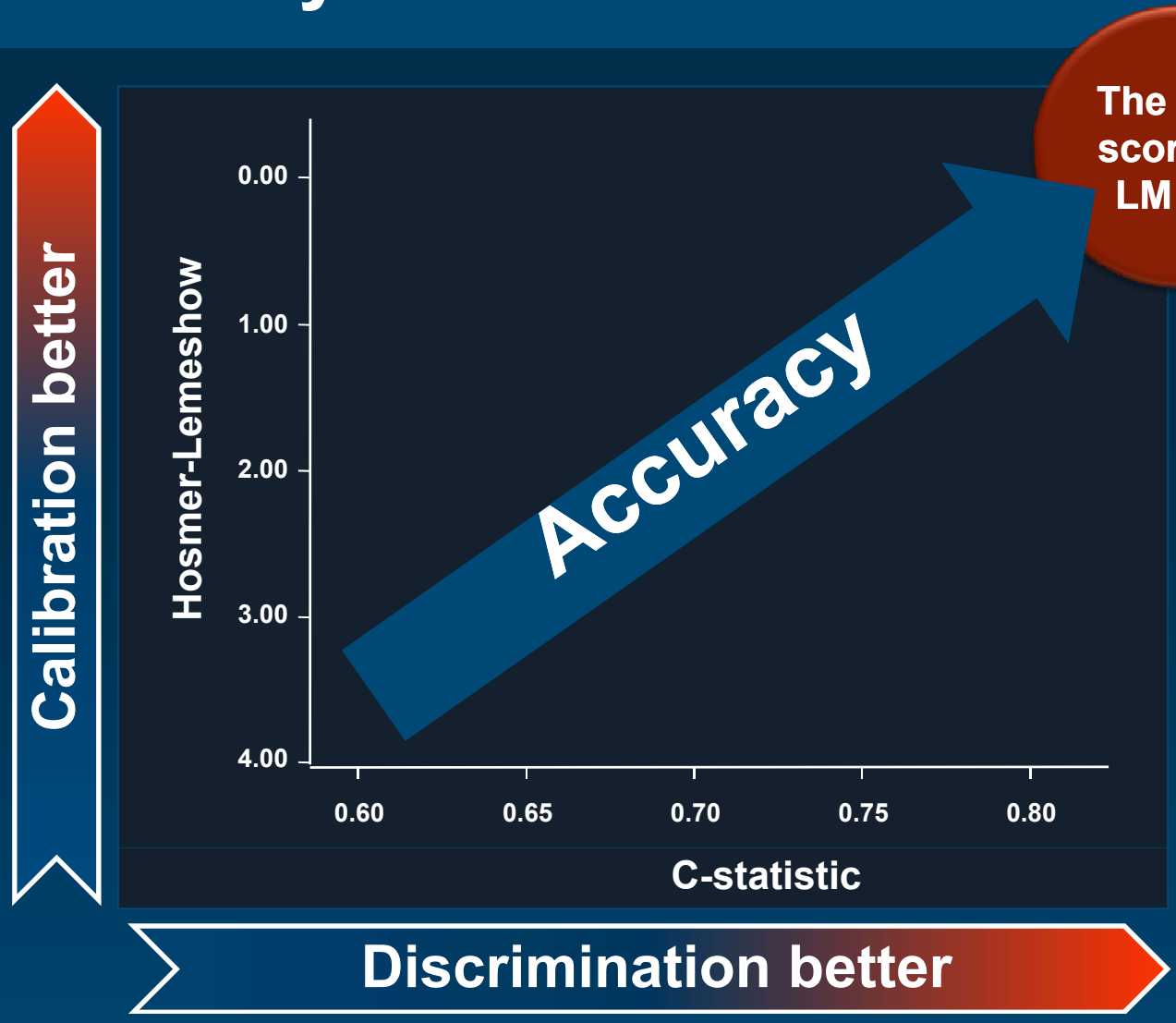
Disclosure Statement of Financial Interest

I, Corrado Tamburino, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

The Ideal Risk Stratification tool

- Easy to apply at the bed-side or in the cath-lab
- Reproducible
- Uses data routinely available before the procedure
- Accurate

Accuracy is a function of two characteristics



Discrimination
Measures how much the score can differentiate between poor and good outcomes

Calibration
Measures how close the estimates are to a real probability

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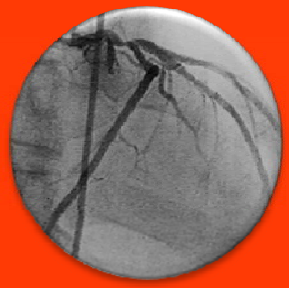
Risk Stratification in LM Disease



Angiographic

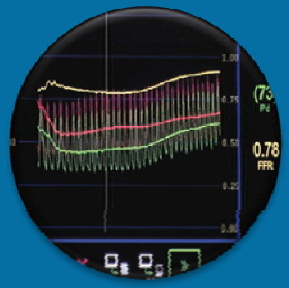
- SYNTAX score (Sxscore)
- Residual SYNTAX score (rSS)*

Clinical

- EuroSCORE
- EuroSCORE 2*
- STS score*
- ACEF score

Combined

- GRC
- CSS
- Logistic CSS*
- NERS



Functional

- Functional SYNTAX score (FSS)*
- Non-invasive FSS*

*not yet presented or validated in LM PCI

Risk Stratification in LM Disease

Angiographic

- SYNTAX score (Sxscore)
- Residual SYNTAX score (rSS)*

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Combined

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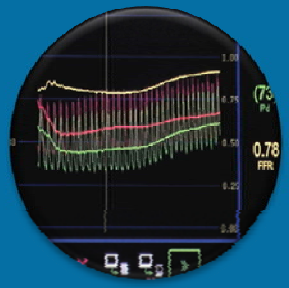
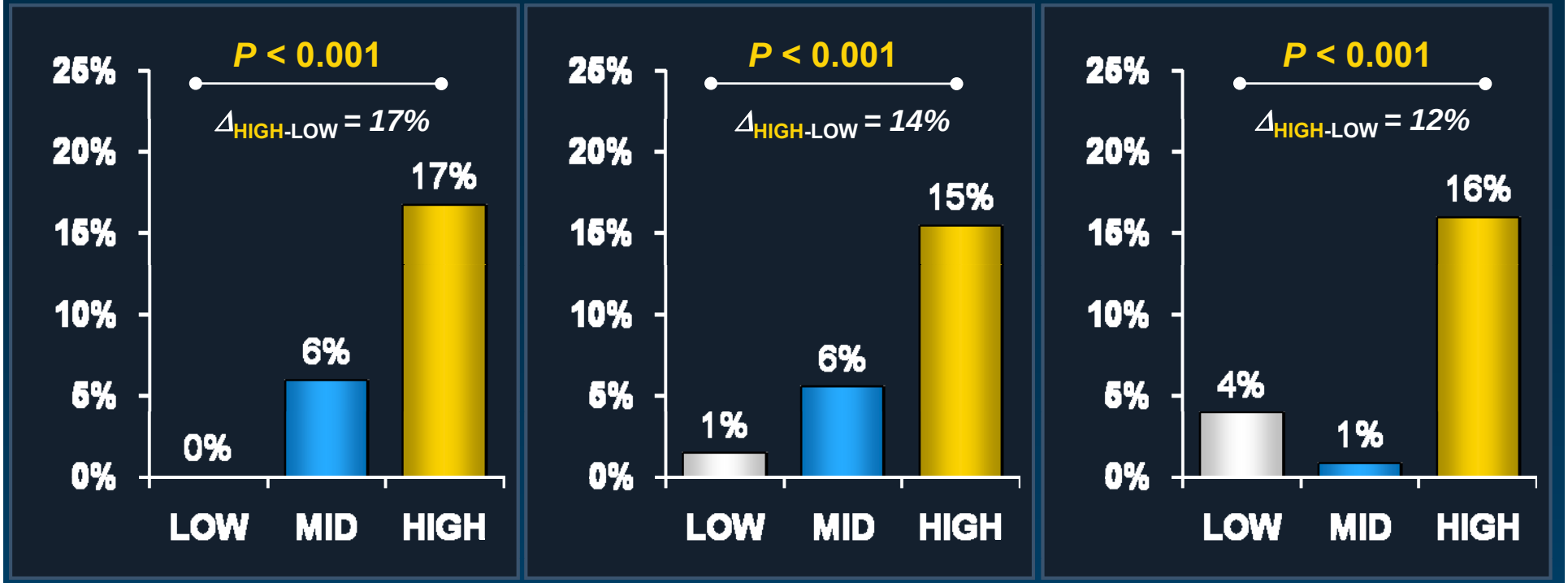


Functional

- Functional SYNTAX score (FSS)*
- Non-invasive FSS*

*not yet presented or validated in LM PCI

Stand-Alone Clinical Scores (ACEF, EuroSCORE) versus SYNTAX score in LM PCI



Hosmer-Lemeshow: 1.607
c-statistic: 0.69

Hosmer-Lemeshow: 0.216
c-statistic : 0.69

Hosmer-Lemeshow: 2.448
c-statistic : 0.73

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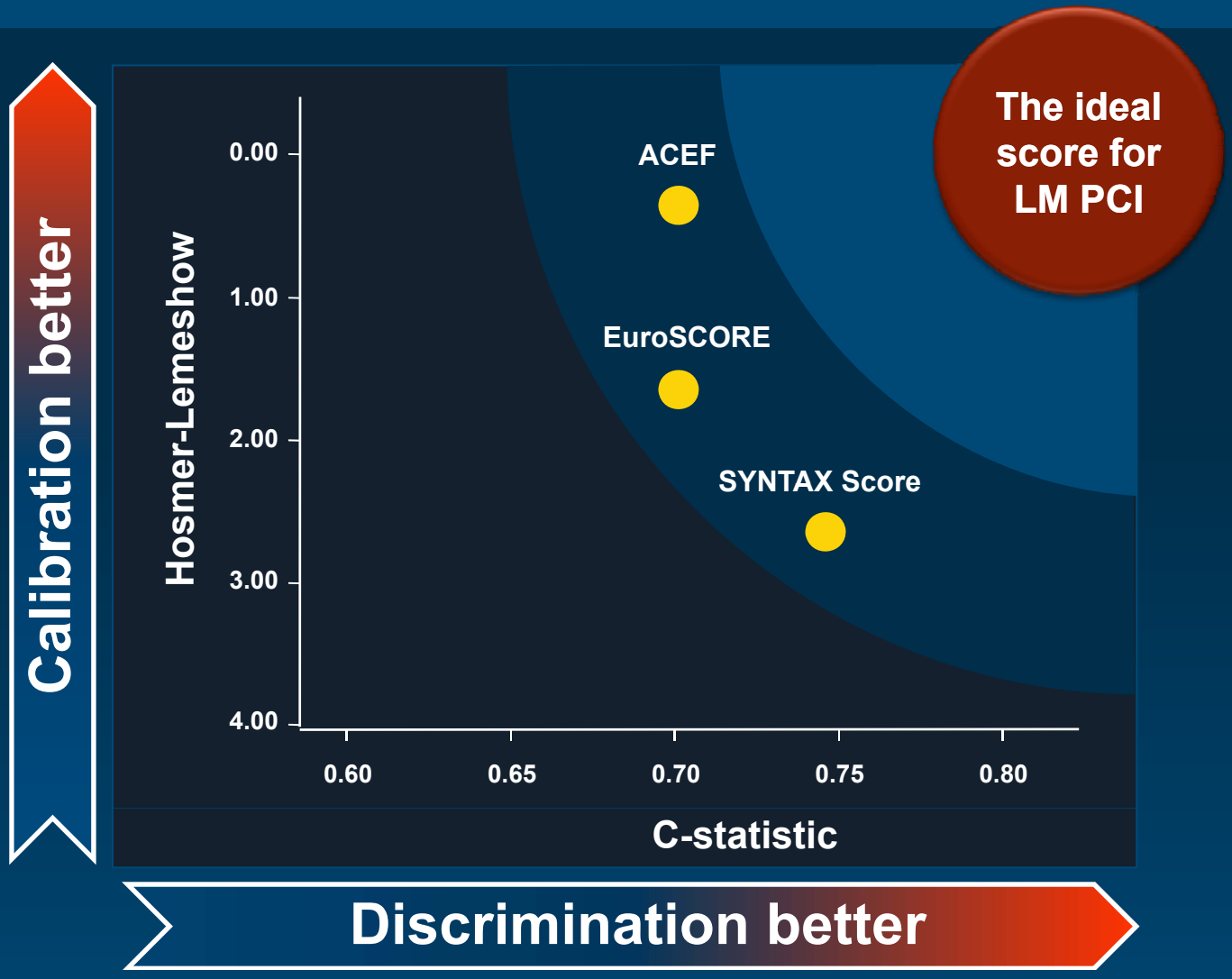
Stand-alone Scores Are Far from Perfection



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Combined Risk models in LM PCI: The best of both worlds?

Angiographic

- SYNTAX score (Sxscore)

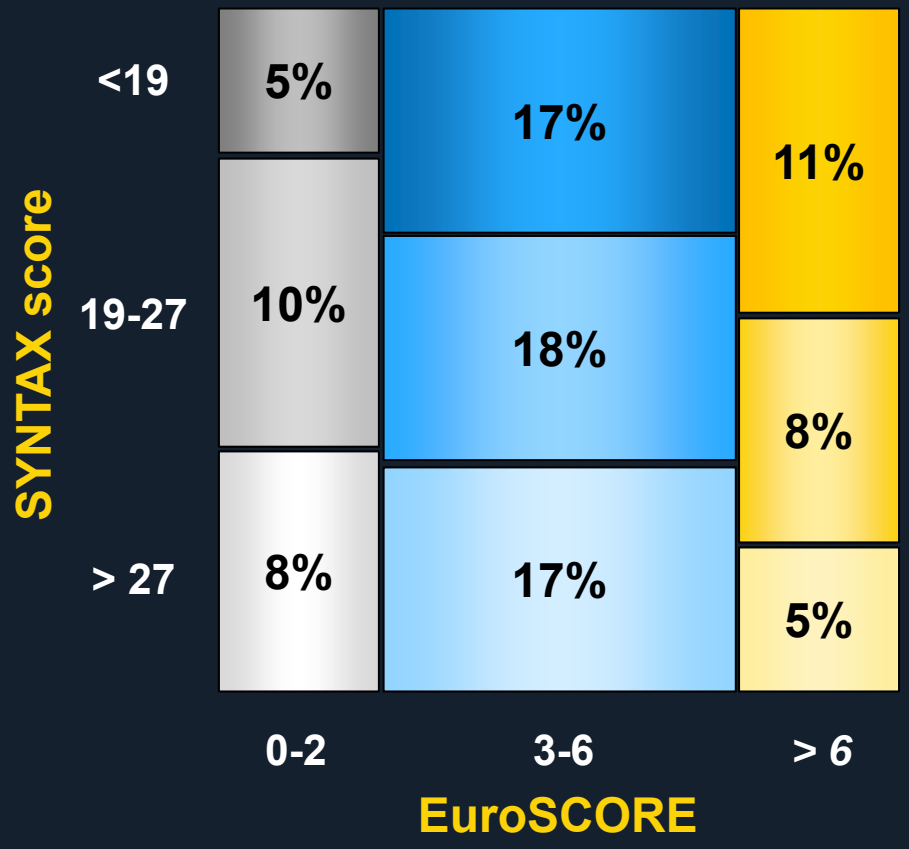
Clinical

- EuroSCORE
- ACEF score

Combined

- NERS
- CSS
- GRC

Angiography is not enough



Clinical and angiographic scores summarize very different information in patients with unprotected LM

Low Spearman rank correlation coefficient between SYNTAX score and EuroSCORE (R_S=0.204, p = 0.001)

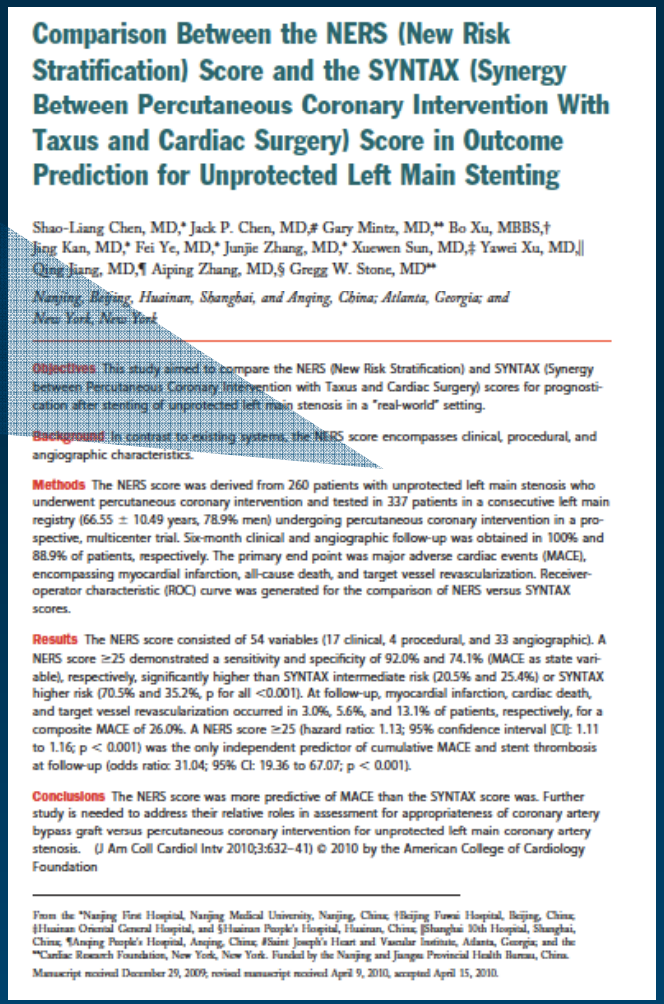
The frequency of patients for each cross-tabulation cell is shown within a rectangle that is proportional in size to the frequency

The New Risk Classification (NERS)

- **Based on 17 clinical, 4 procedural, and 33 angiographic variables**
- **Better discriminates a broad array of endpoints than SYNTAX score, including MACE, Death, MI, TVR and ST in patients undergoing LM PCI**

Background

The potential contributions of clinical, procedural, and angiographic indices in LM patients have not been fully elucidated



Comparison Between the NERS (New Risk Stratification) Score and the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score in Outcome Prediction for Unprotected Left Main Stenting

Shao-Liang Chen, MD,* Jack P. Chen, MD,# Gary Mintz, MD,** Bo Xu, MBBS,† Jing Kan, MD,* Fei Ye, MD,* Junjie Zhang, MD,* Xuewen Sun, MD,‡ Yawei Xu, MD,‖ Qing Jiang, MD,¶ Aiping Zhang, MD,§ Gregg W. Stone, MD**

Nanjing, Beijing, Huainan, Shanghai, and Anqing, China; Atlanta, Georgia; and New York, New York

Objectives This study aimed to compare the NERS (New Risk Stratification) and SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) scores for prognostication after stenting of unprotected left main stenosis in a "real-world" setting.

Background In contrast to existing systems, the NERS score encompasses clinical, procedural, and angiographic characteristics.

Methods The NERS score was derived from 260 patients with unprotected left main stenosis who underwent percutaneous coronary intervention and tested in 337 patients in a consecutive left main registry (66.55 ± 10.49 years, 78.9% men) undergoing percutaneous coronary intervention in a prospective, multicenter trial. Six-month clinical and angiographic follow-up was obtained in 100% and 88.9% of patients, respectively. The primary end point was major adverse cardiac events (MACE), encompassing myocardial infarction, all-cause death, and target vessel revascularization. Receiver-operator characteristic (ROC) curve was generated for the comparison of NERS versus SYNTAX scores.

Results The NERS score consisted of 54 variables (17 clinical, 4 procedural, and 33 angiographic). A NERS score ≥25 demonstrated a sensitivity and specificity of 92.0% and 74.1% (MACE as state variable), respectively, significantly higher than SYNTAX intermediate risk (20.5% and 25.4%) or SYNTAX higher risk (70.5% and 35.2%, p for all <0.001). At follow-up, myocardial infarction, cardiac death, and target vessel revascularization occurred in 3.0%, 5.6%, and 13.1% of patients, respectively, for a composite MACE of 26.0%. A NERS score ≥25 (hazard ratio: 1.13; 95% confidence interval [CI]: 1.11 to 1.16; $p < 0.001$) was the only independent predictor of cumulative MACE and stent thrombosis at follow-up (odds ratio: 31.04; 95% CI: 19.36 to 67.07; $p < 0.001$).

Conclusions The NERS score was more predictive of MACE than the SYNTAX score was. Further study is needed to address their relative roles in assessment for appropriateness of coronary artery bypass graft versus percutaneous coronary intervention for unprotected left main coronary artery stenosis. (J Am Coll Cardiol Intv 2010;3:632–41) © 2010 by the American College of Cardiology Foundation

From the *Nanjing First Hospital, Nanjing Medical University, Nanjing, China; †Beijing Fuwai Hospital, Beijing, China; ‡Huainan Oriental General Hospital, and §Huainan People's Hospital, Huainan, China; ‖Shanghai 10th Hospital, Shanghai, China; ¶Anqing People's Hospital, Anqing, China; #Saint Joseph's Heart and Vascular Institute, Atlanta, Georgia; and the **Cardiac Research Foundation, New York, New York. Funded by the Nanjing and Jiangsu Provincial Health Bureau, China.

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Caveats of NERS

- Labor-intensive
  - 54 variables
- Overfitted
  - 126 variables tested in 260 patients
- No prospective validation
- Utility in decision-making remains uncertain
  - Does include procedural variables, cannot be calculated upfront

Clinical SYNTAX score (CSS)

- **Calculated as SYNTAX score*modified ACEF score**
- **Better discriminates 5-Year Death and MACE in multivessel CAD than SYNTAX score**
- **Better discriminates 5-Year Death in All-Comers PCI**

Background

Being solely based on angiographic variables, the SYNTAX score cannot account for the variability related to clinical factors which are widely acknowledged to impact on long-term outcomes

A New Tool for the Risk Stratification of Patients With Complex Coronary Artery Disease

The Clinical SYNTAX Score

Scot Garg, MB, ChB, MRCP; Giovanna Sarno, MD, PhD; Hector M. Garcia-Garcia, MD, PhD; Chrysafios Girasis, MD; Joanna Wykrzykowska, MD; Keith D. Dawkins, MD; Patrick W. Serruys, MD, PhD; on behalf of the ARTS-II Investigators

Background—Presently, no effective risk model exists to predict long-term mortality or other major adverse cardiovascular and cerebrovascular events (MACCE) in those patients undergoing percutaneous coronary intervention (PCI). This study aimed to assess whether the Clinical SYNTAX Score (CSS) calculated by multiplying the SYNTAX Score to a modified ACEF score (age/ejection fraction +1 for each 10 mL the creatinine clearance <60 mL/min per 1.73 m^2) would improve the ability of either score to predict mortality and MACCE.

Methods and Results—The CSS was calculated in 512 patients enrolled in the ARTS-II study who had serum creatinine levels, ejection fraction, and body weight recorded at baseline. Clinical outcomes in terms of MACCE and mortality at 1- and 5-year follow-up were stratified according to CSS tertiles: $CSS_{LOW} \leq 15.6$ (n=170), $15.6 < CSS_{MID} \leq 27.5$ (n=171), and $CSS_{HIGH} > 27.5$ (n=171). At 1-year follow-up, rates of repeat revascularization and MACCE were significantly higher in the highest tertile group. At 5-year follow-up, CSS_{HIGH} had a comparable rate of myocardial infarction, a trend toward a significantly higher rate of death, and significantly higher rates of repeat revascularization and overall MACCE compared with patients in the lower 2 tertiles. The respective C-statistics for the CSS, SYNTAX Score, and ACEF score for 5-year mortality were 0.69, 0.62, and 0.65 and for 5-year MACCE were 0.62, 0.59, and 0.57.

Conclusions—An improvement in the ability of the SYNTAX Score to predict MACCE and mortality can be achieved by combining the SYNTAX Score with a simple clinical risk score incorporating age, ejection fraction, and creatinine clearance to produce the Clinical SYNTAX score.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00235170.

(*Circ Cardiovasc Interv*. 2010;3:317-326.)

Key Words: SYNTAX score ■ complex coronary artery disease ■ risk stratification

Coronary artery bypass grafting (CABG) has historically been the preferred method of revascularization in patients with complex coronary artery disease (CAD); however, recent evidence indicates that in specific groups of patients, percutaneous coronary intervention (PCI) can offer a safe and suitable alternative.[1–4] This expanding use of PCI[5] has consequently increased the importance of developing a systematic approach for risk stratifying these complex patients so that they might receive the appropriate revascularization option. The ability to objectively decide which patients with complex CAD are suitable for PCI has gained new ground recently after the introduction of the SYNTAX Score.[6,7] Not only can this lesion-based scoring system quantify coronary anatomic complexity, but studies also demonstrate that it has a role in the short- and long-term risk stratification of patients undergoing PCI.[1,4,8–11]

Clinical Perspective on p 326

One of the limitations of using the SYNTAX Score in this context is that lesion-based scoring systems have been shown to have a lower ability to predict mortality when compared with scoring systems using clinical characteristics.[12] In patients undergoing PCI, there are currently only limited data available on the use of risk scores that rely solely on clinical characteristics, such as the euroSCORE.[13–15] Moreover, it has been suggested that the use of too many individual variables may reduce the overall accuracy of data.[16] The recently introduced ACEF score, for example, uses just age, left ventricular ejection fraction (LVEF), and serum creatinine (SCr) and appears to be as good as more complex scores in predicting mortality in patients undergoing elective CABG.[17] An acceptable modification to the ACEF score is to use the

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The online-only Data Supplement is available at http://circinterventions.ahajournals.org/cgi/content/full/CIRCINTERVENTIONS.109.914051/DC1.

Correspondence to Patrick W. Serruys, MD, PhD, Ba583a, Thoraxcentre, Erasmus MC, 's-Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands. E-mail p.w.j.c.serruys@erasmusmc.nl

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Circ Cardiovasc Interv is available at http://circinterventions.ahajournals.org DOI: 10.1161/CIRCINTERVENTIONS.109.914051

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Garg S et al. *Circ Card Interv* 2010;3:317-26
Girasis C et al. *Eur Heart J* 2011;32:3115-27

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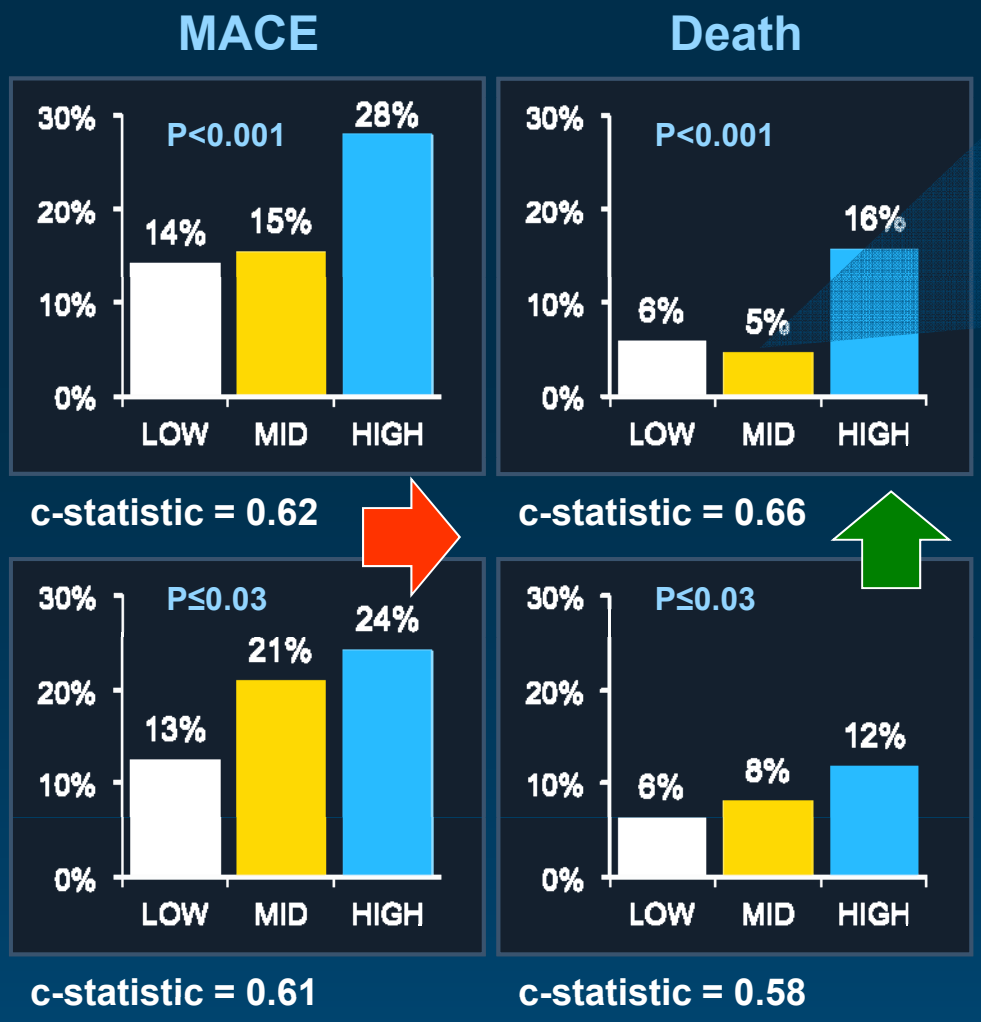
CSS – No improvement in discrimination of MACE vs. SYNTAX score. Better discrimination in mortality, but limitations remain

CSS

17.4±20.5

SYNTAX score

11.7±7.3



- Tertiles are not in the anticipated order
- Modest gain in calibration vs SYNTAX score (|2 8 vs 6)

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Nam CW et al. *J Am Coll Cardiol* 2011;58:1211-8

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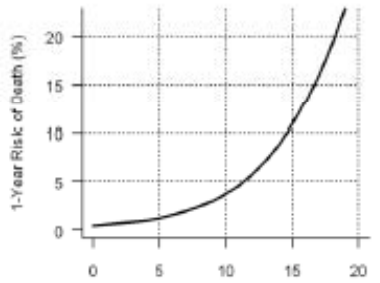
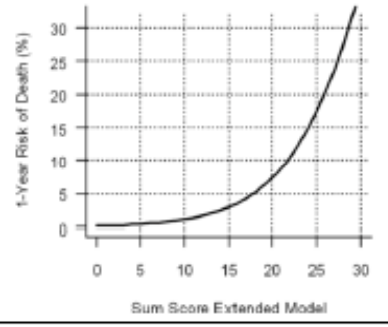
Logistic Clinical SYNTAX Score

	Points	Score
SYNTAX Score	see below	
Age (years)	see below	
CrCl (ml/min)	see below	
LV Ejection Fraction	see below	
'SYNTAX' Patient*	3	
Sum Score Core Model		
STEMI	3	
NSTEMI	4	
BMI	see below	
PVD	3	
Insulin Treated DM	4	
Non Insulin DM	2	
Previous MI	2	
Current smoking	2	
Sub Score Added Predictors		+
Sum Score Extended Model		





SYNTAX Score	≤ 17	18-22	23-27	28-32	≥ 33			
	0	1	2	3	4			
Age (years)	< 50	50-54	55-59	60-64	65-69	70-74	75-79	≥80
	0	1	2	3	4	5	6	7
CrCl (ml/min)	< 30	30-59	60-89	≥90				
	3	2	1	0				
LV Ejection Fraction (%)	< 30	30-34	35-39	40-44	45-49	≥50		
	10	8	6	4	2	0		
BMI (kg/m^2)	<20	21-24	25-29	30-34	≥ 35			
	0	1	2	3	4			

*SYNTAX Patient defined as fulfilling the enrolment criteria for the SYNTAX All-Comers trial i.e. left main stem (isolated or associated with one, two or three vessel disease) or three vessel disease alone.

Serruys PW, ACC 2012

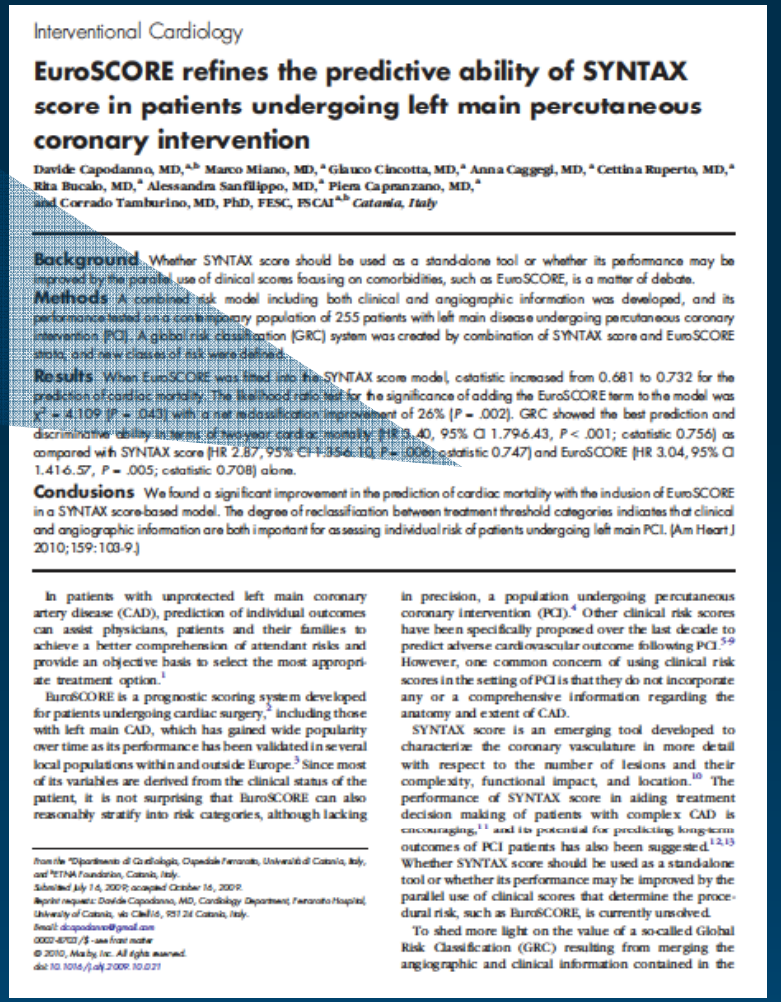
AMERICAN COLLEGE OF CARDIOLOGY

Global Risk Classification (GRC)

- **Developed as an Integration of the SYNTAX score and the EuroSCORE**
- **Better discriminates in-hospital and 2-Year Cardiac Death in LM PCI than SYNTAX score alone**

Conclusions

Incorporation of clinical risk factors and comorbidities into existing estimation systems may refine their prognostic ability and guide clinical decisions



Interventional Cardiology

EuroSCORE refines the predictive ability of SYNTAX score in patients undergoing left main percutaneous coronary intervention

Davide Capodanno, MD,[a,b] Marco Miano, MD,[a] Glauco Cincotta, MD,[a] Anna Caggegi, MD,[a] Cettina Ruperto, MD,[a] Rita Bucalo, MD,[a] Alessandra Sanfilippo, MD,[a] Piera Capranzano, MD,[a] and Corrado Tamburino, MD, PhD, FESC, FSCAI[a,b] *Catania, Italy*

Background Whether SYNTAX score should be used as a stand-alone tool or whether its performance may be improved by the parallel use of clinical scores focusing on comorbidities, such as EuroSCORE, is a matter of debate.

Methods A combined risk model including both clinical and angiographic information was developed, and its performance tested in a contemporary population of 255 patients with left main disease undergoing percutaneous coronary intervention (PCI). A global risk classification (GRC) system was created by combination of SYNTAX score and EuroSCORE scores, and new classes of risk were defined.

Results When EuroSCORE was fitted into the SYNTAX score model, c-statistic increased from 0.681 to 0.732 for the prediction of cardiac mortality. The likelihood ratio test for the significance of adding the EuroSCORE term to the model was $\chi^2 = 4.109$ ($P = .043$) with a net reclassification improvement of 26% ($P = .002$). GRC showed the best prediction and discriminative ability in terms of in-hospital cardiac mortality (HR 8.40, 95% CI 1.796-43, $P < .001$; c-statistic 0.756) as compared with SYNTAX score (HR 2.87, 95% CI 1.356-10, $P = .006$; c-statistic 0.747) and EuroSCORE (HR 3.04, 95% CI 1.416-57, $P = .005$; c-statistic 0.708) alone.

Conclusions We found a significant improvement in the prediction of cardiac mortality with the inclusion of EuroSCORE in a SYNTAX score-based model. The degree of reclassification between treatment threshold categories indicates that clinical and angiographic information are both important for assessing individual risk of patients undergoing left main PCI. (Am Heart J 2010;159:103-9.)

In patients with unprotected left main coronary artery disease (CAD), prediction of individual outcomes can assist physicians, patients and their families to achieve a better comprehension of attendant risks and provide an objective basis to select the most appropriate treatment option.[1]

EuroSCORE is a prognostic scoring system developed for patients undergoing cardiac surgery,[2] including those with left main CAD, which has gained wide popularity over time as its performance has been validated in several local populations within and outside Europe.[3] Since most of its variables are derived from the clinical status of the patient, it is not surprising that EuroSCORE can also reasonably stratify into risk categories, although lacking in precision, a population undergoing percutaneous coronary intervention (PCI).[4] Other clinical risk scores have been specifically proposed over the last decade to predict adverse cardiovascular outcome following PCI.[5-9] However, one common concern of using clinical risk scores in the setting of PCI is that they do not incorporate any or a comprehensive information regarding the anatomy and extent of CAD.

SYNTAX score is an emerging tool developed to characterize the coronary vasculature in more detail with respect to the number of lesions and their complexity, functional impact, and location.[10] The performance of SYNTAX score in aiding treatment decision making of patients with complex CAD is encouraging,[11] and its potential for predicting long-term outcomes of PCI patients has also been suggested.[12,13] Whether SYNTAX score should be used as a stand-alone tool or whether its performance may be improved by the parallel use of clinical scores that determine the procedural risk, such as EuroSCORE, is currently unsolved.

To shed more light on the value of a so-called Global Risk Classification (GRC) resulting from merging the angiographic and clinical information contained in the

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Capodanno D et al. *Am Heart J* 2010;159:103-9

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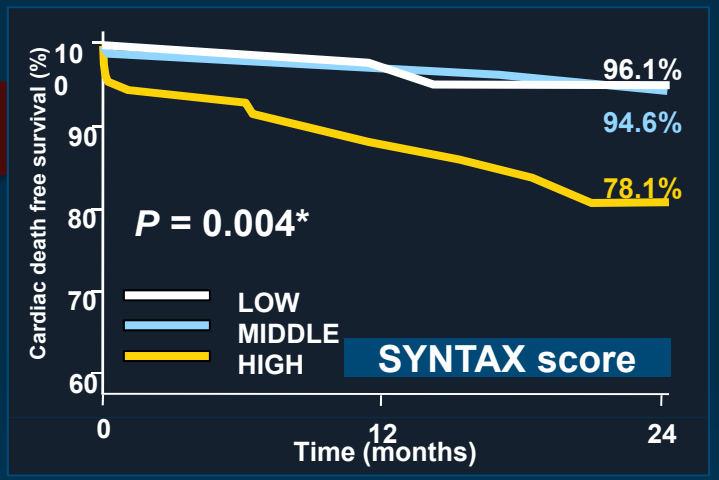
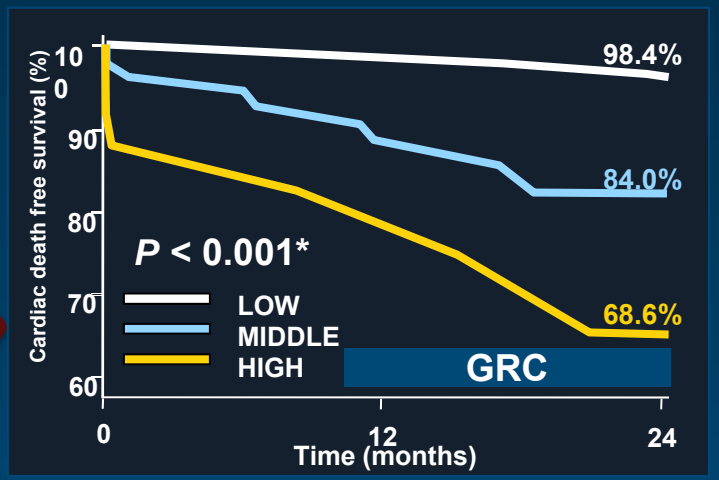
GRC – Prognostic ability in improving both discrimination and calibration vs SYNTAX score

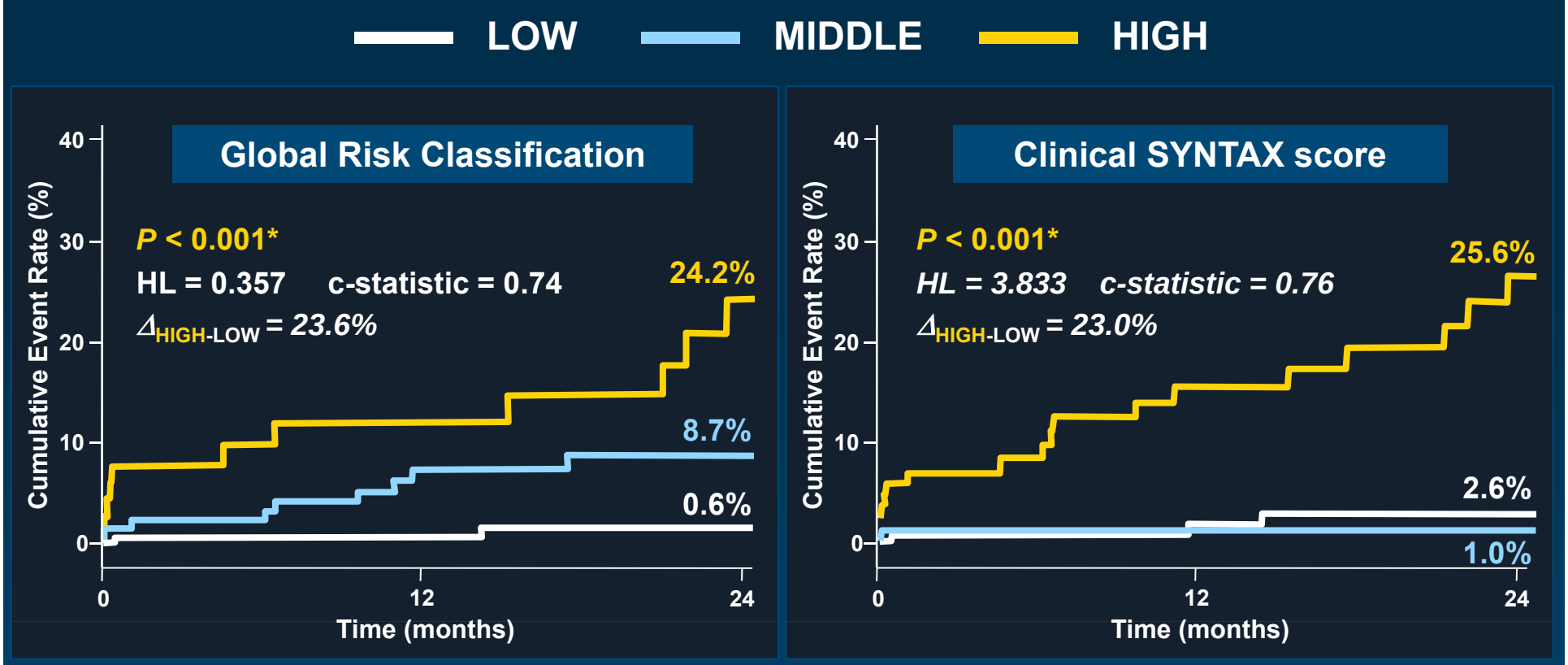
EuroSCORE	SYNTAX score <19	SYNTAX score 19-27	SYNTAX score >27
0-2	L	L	I
3-6	L	L	I
> 6	I	I	H





* log rank test;
n = 255 LM patients undergoing PCI

Cardiac death to 2 Years by stratification of GRC and CSS in LM PCI (N = 400)



* log rank test; higher HL (Hosmer-Lemeshow) statistic indicates poorer calibration; higher $\Delta_{HIGH-LOW}$ (Index of separation) indicates better discrimination

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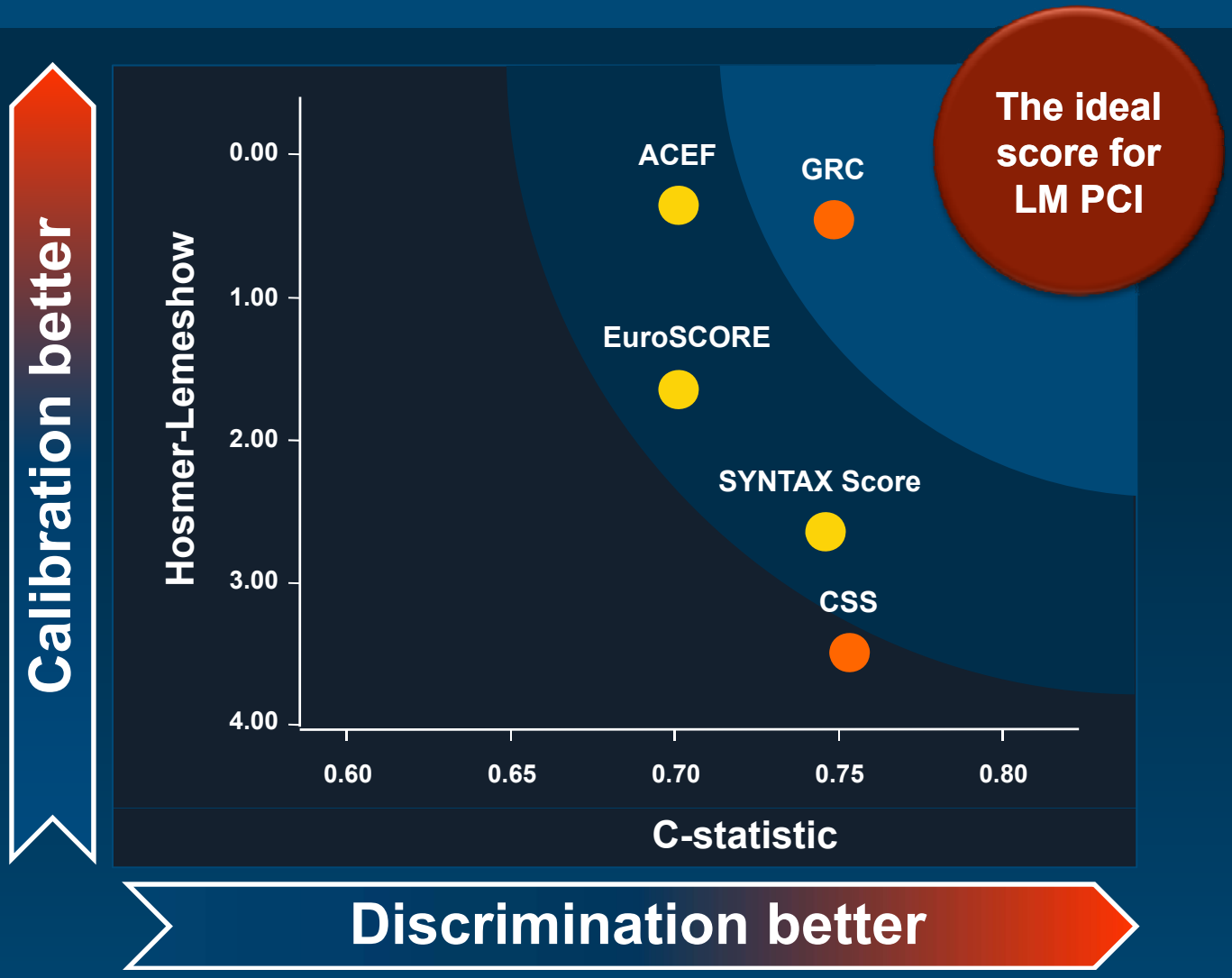
GRC approaches the ideal model for LM PCI



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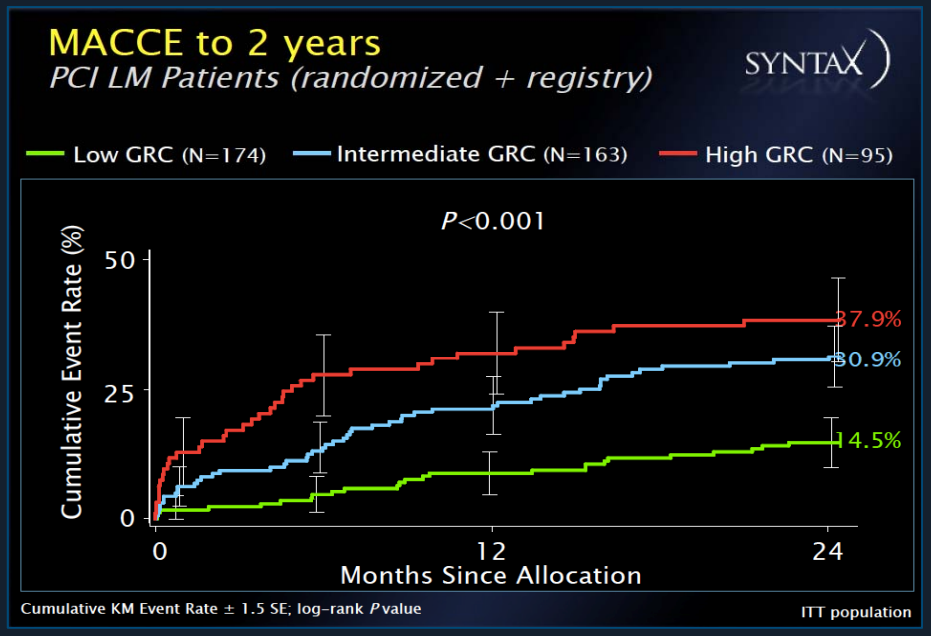
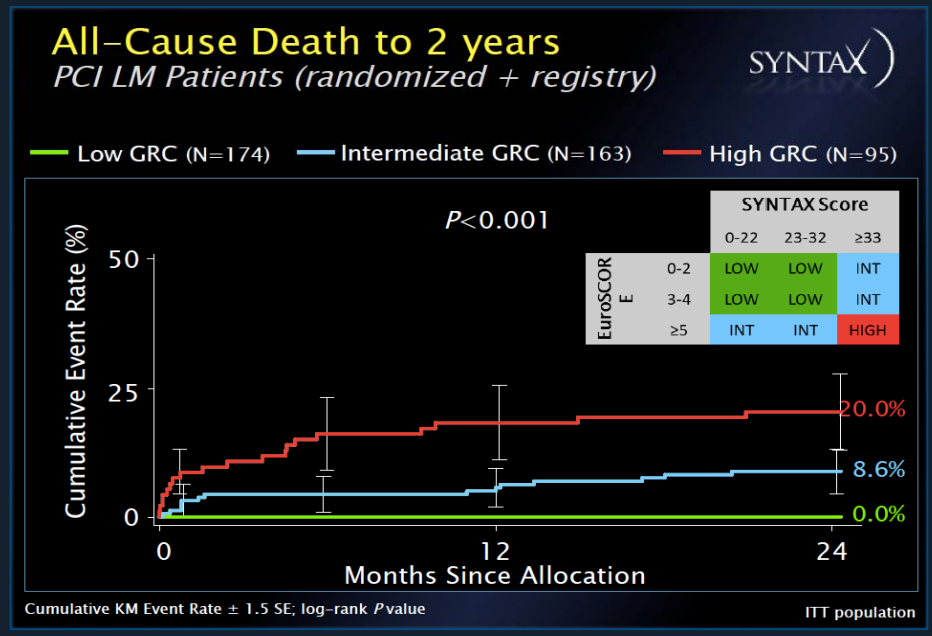
Lessons on the GRC from the SYNTAX trial

MACCE



- Improved MACCE stratification

Death



- Excellent mortality stratification

The GRC may help to identify a population at very low risk of events after LM PCI

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Serruys et al., presented at LM Summit 2011

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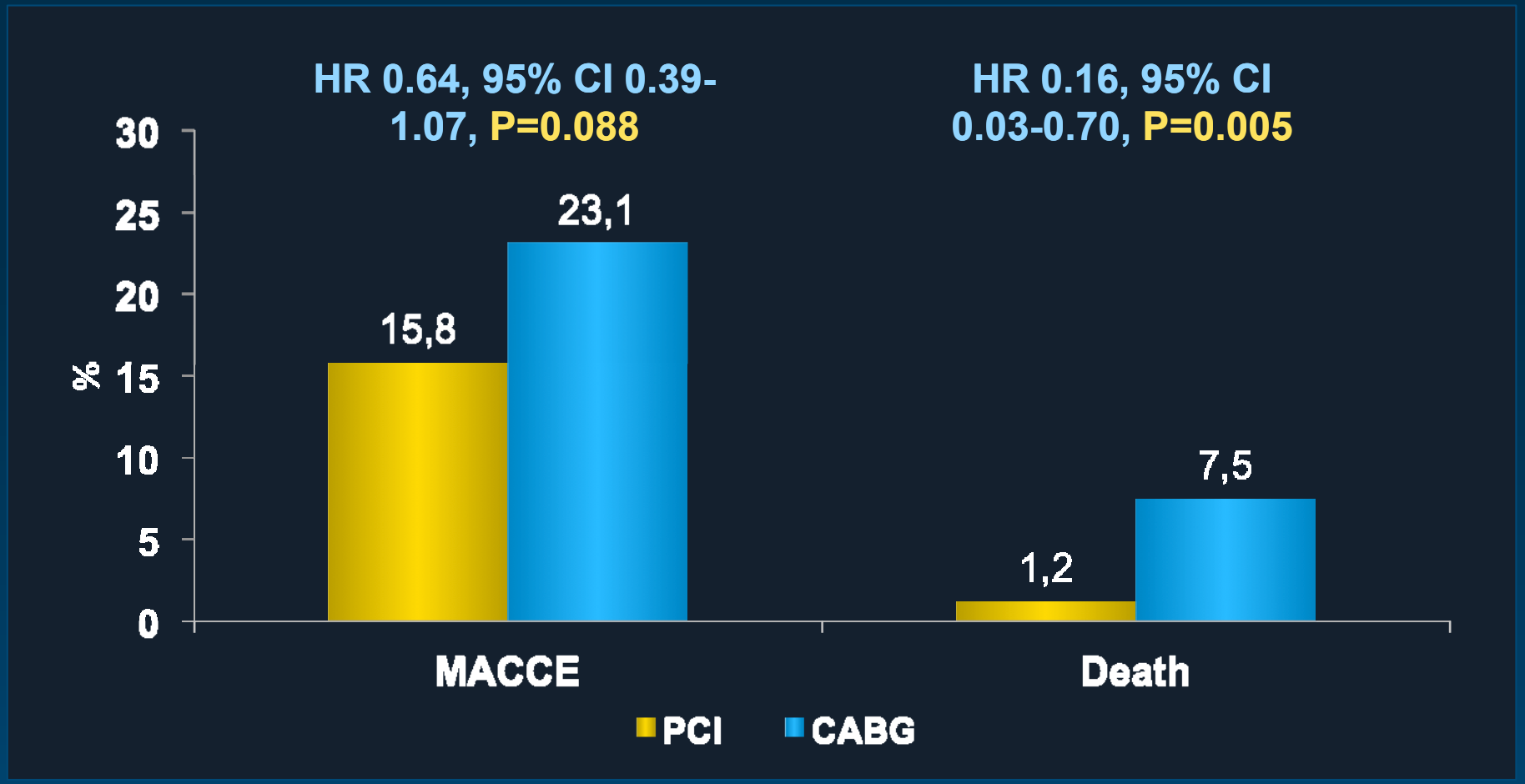
PCI vs CABG in LM Patients with Low GRC in the SYNTAX Trial at 3 Years



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Serruys et al. *J Am Coll Cardiol* 2011;58:87 (abstract)

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Decision-making based on the Global Risk Classification

EuroSCORE	SYNTAX score ≤22	SYNTAX score 22-32	SYNTAX score ≥32
0-2	PCI	PCI	?
3-5	PCI	PCI	?
≥6	?	?	CABG

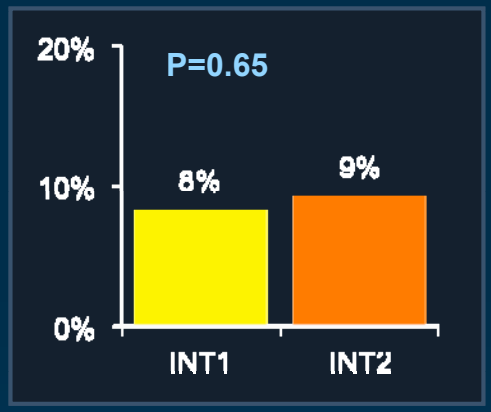
The comparative role of PCI and CABG in LM patients in the intermediate GRC risk group (≈40%) is not well defined

Decision-making based on the Global Risk Classification: cardiac death

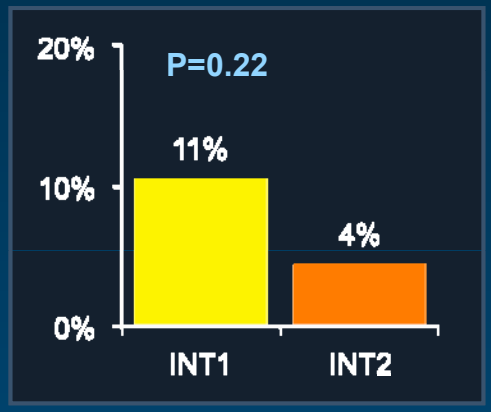
EuroSCORE	SYNTAX score ≤22	SYNTAX score 22-32	SYNTAX score ≥32
0-2	PCI	PCI	INT_2
3-5	PCI	PCI	INT_2
≥6	INT_1	INT_1	CABG

INT_1 = high clinical/acceptable angiographic risk
INT_2 = acceptable clinical/high angiographic risk

PCI



CABG



Decision-making based on the Global Risk Classification

EuroSCORE	SYNTAX score ≤22	SYNTAX score 22-32	SYNTAX score ≥32
0-2	**PCI**	**PCI**	**CABG**
3-5	**PCI**	**PCI**	**CABG**
≥6	**PCI /CABG**	**PCI /CABG**	**CABG**

Performing CABG in patients with SYNTAX score ≥32 complies with guidelines

The efficacy and safety of performing PCI in patients with SYNTAX score <33 will be addressed by the EXCEL trial

Conclusions

- **Risk stratification** in LM PCI aims to govern the unpredictability of random variation
- Risk estimation and classification are best achieved by integrating **clinical**, **angiographic** and **functional** information
- With multiplication of risk scoring systems and modifications from existing models, **expert consensus** on how to use these tools for decision-making is **essential** to avoid a "Tower of Babel" effect