

## SUPPLEMENTAL MATERIAL

### 1. C-statistics and reclassification analysis for hard events

The sensitivity of the results (i.e. Cox model-fitting and reclassification from the models) for hard events (N=7: cardiac death and nonfatal myocardial infarction) were evaluated.

While the small event number (n=7) made all confidence intervals extremely wide, point estimates lay in the same direction as those from the original soft-endpoint analysis. Although the hazard ratio estimates for "CACCS >400 vs. <400" appear too large (8-9 times), wide confidence intervals also suggested uncertainty due to the small event number, which is the limitation of our data. C-statistics and reclassification analysis also suggested that predictive accuracy for hard event could be improved by adding CACS and non-culprit CT-HRP (Table1-3). These results should be accepted carefully, however, for slight change in a data pattern can strongly influence the results (i.e. Cox model estimates, consequently C-stats and reclassification indexes) in data with the limited number of events.

Table 1. Association and prediction measures from the three candidate Cox models for "hard" cardiac events (death and MI)

	Model 1	Model 2	Model 3
	Hazard ratio ratio (95% confidence interval)		
Age (per year)	0.944 (0.871, 1.024)	0.921 (0.844, 1.006)	0.925 (0.845, 1.012)
Diabetes (vs. none)	0.711 (0.137, 3.683)	0.469 (0.085, 2.576)	0.518 (0.095, 2.826)
Triglyceride (per 10 mg/dl)	0.971 (0.884, 1.066)	0.960 (0.876, 1.051)	0.961 (0.871, 1.059)
CACS 100-400 (vs. <400)		1.542 (0.090, 26.376)	1.572 (0.093, 26.591)
CACS >400 (vs. <400)		9.347 (0.961, 90.920)	8.425 (0.897, 79.125)
Non-culprit CT-HRP (vs. none)			3.414 (0.646, 18.046)
Harrell's c, % (bootstrap SE)*	57.48 (10.63)	77.10 (9.23)	83.97 (4.34)
Two-sided <i>p</i> for c-increment*†		0.056	0.124
Minus-2 times log likelihood	77.0	70.7	69.0
Likelihood ratio <i>p</i> †		0.043	0.427
AIC, Akaike's Information Criterion; FRS, Framingham Risk Score			
* Based on 500 bootstrap samples			
† Comparison between adjacent models using bootstrap SE (Models 1 vs. 2 or Models 2 vs. 3)			

Table 2. Reclassification tables by predicted 1,000-day "hard" cardiac risks from the Cox models between Model 1 and Model 2

	Model 2			
Model 1	<1%	1%-<3%	3%-<5%	5%-
	Non-events, <i>n</i> (%)			
<1%	7.0 (2.1)	7.0 (2.1)		
1%-<3%	<b>128.0 (39.1)</b>	55.0 (16.8)	17.0 (5.2)	29.8 (9.1)
3%-<5%	<b>5.0 (1.5)</b>	<b>45.0 (13.8)</b>	1.0 (0.3)	15.0 (4.6)
5%-		<b>5.0 (1.5)</b>	<b>9.0 (2.8)</b>	3.3 (1.0)
	Events, <i>n</i> (%)			
<1%	0.0 (0.0)			
1%-<3%	1.0 (12.7)	1.0 (12.7)	<b>1.0 (12.7)</b>	<b>2.2 (27.9)</b>
3%-<5%			0.0 (0.0)	
5%-				2.7 (33.9)
<b>Bold numbers</b> indicate improved reclassifications, while <i>Italicized numbers</i>				
$NRI_{\text{Non-Event}} = 39.1 + 1.5 + 13.8 + 1.5 + 2.8 - 2.1 - 5.2 - 9.1 - 4.6 = 37.7\%$				
$NRI_{\text{Event}} = 12.7 + 27.9 - 12.7 = 27.9\%$				
$NRI = 37.7 + 27.9 = 65.6\%$				
Category-free NRI = 90.0% (event: 51.8%, non-event: 38.2%)				

Table 3. Reclassification tables by predicted 1,000-day "hard" cardiac risks from the Cox models between Model 2 and Model 3

Model 2	Model 3			
	<1%	1%-<3%	3%-<5%	5%-
	Non-events, <i>n</i> (%)			
<1%	126.0 (38.6)	<i>14.0 (4.3)</i>		
1%-<3%	<b>21.0 (6.4)</b>	89.0 (27.2)	<i>2.0 (0.6)</i>	
3%-<5%		<b>8.0 (2.4)</b>	17.0 (5.2)	<i>2.0 (0.6)</i>
5%-			<b>15.8 (4.8)</b>	32.0 (9.8)
	Events, <i>n</i> (%)			
<1%	0.0 (0.0)	<b>1.0 (12.2)</b>		
1%-<3%		1.0 (12.2)	<b>1.0 (12.2)</b>	
3%-<5%			0.0 (0.0)	
5%-			<i>1.2 (14.8)</i>	4.0 (48.7)
<b>Bold numbers</b> indicate improved reclassifications, while <i>Italicized numbers</i>				
$NRI_{\text{Non-Event}} = 6.4 + 2.4 + 4.8 - 4.3 - 0.6 - 0.6 = 8.7\%$				
$NRI_{\text{Event}} = 12.2 + 12.2 - 14.8 = 9.6\%$				
$NRI = 8.7 + 9.6 = 18.3\%$				
Category-free NRI = 27.0% (event: -54.7%, non-event: 81.7%)				

## 2. Reclassification by predicted 1000-day risks from different models, reclassification tables using Net reclassification indices (NRI)

For reclassification by predicted 1000-day risks from different models, reclassification tables for survival data that used expected rather than actual event numbers for each cell were presented separately for event and nonevent. Net reclassification indices (NRIs) were calculated according to the reclassification tables

Reclassification tables of the model with CACS (Model 2) vs. the model including neither CACS nor CT-HRP (Model 1), and the model with both CACS and CT-HRP (Model 3) vs. the model with CACS (Model 2) are presented in Tables 4 and 5, respectively. We adopted four levels of risk-classification (<20%, 20% to <30%, 30% to <40%, 40%≤) within 1000 days. CACS improved the classification compared to the model without it (NRI = 12.7% [difference between the percentages of bold numbers and of italicized numbers]) and CT-HRP added to CACS further improved the classification (NRI = 6.9%). These findings suggest that more subjects were correctly than incorrectly reclassified by adding CACS and CT-HRP into prognostic models.

Table 4. Reclassification tables by predicted 1,000-day cardiac risks from the Cox models between Model 1 and Model 2

Predicted Risk from Model 1	Predicted Risk from Model 2				Total
	<20%	20%-<30%	30%-<40%	40%-	
Expected Number in Non-events*, <i>n</i> (%)					
<20%	1.0 (0.5)	2.0 (0.9)			
20%-<30%	<b>51.7 (23.7)</b>	39.9 (18.3)	<i>34.4 (15.8)</i>		
30%-<40%		<b>21.7 (10.0)</b>	10.5 (4.8)	<i>19.8 (9.1)</i>	
40%-		<b>12.0 (5.5)</b>	<b>0 (0.0)</b>	24.9 (11.4)	
Total					217.9 (100.0)
Expected Number in Events*, <i>n</i> (%)					
<20%	0 (0.0)	<b>1.0 (0.9)</b>			
20%-<30%	<i>3.3 (2.8)</i>	16.1 (13.7)	<b>4.3 (3.7)</b>		
30%-<40%		<i>4.3 (3.7)</i>	11.5 (9.9)	<b>13.2 (11.3)</b>	
40%-		<i>7.0 (6.0)</i>	<i>7.0 (6.0)</i>	37.1 (31.7)	
Total					117.1 (100.0)

**Bold numbers** indicate improved reclassifications, while *Italicized numbers* indicate worsened reclassifications by adding CACS categories to the Model 1.

\* Expected numbers were calculated by the Kaplan-Meier method in subgroups defined by the combination of the predicted risk-categories from Model 1 and Model 2.

Table 5. Reclassification tables by predicted 1,000-day cardiac risks from the Cox models between Model 2 and Model 3

Predicted Risk from Model 2	Predicted Risk from Model 3				Total
	<20%	20%-<30%	30%-<40%	40%-	
Expected Number in Non-events*, <i>n</i> (%)					
<20%	49.7 (22.3)	<i>1.0 (0.4)</i>	<i>2.0 (0.9)</i>		
20%-<30%	<b>7.0 (3.1)</b>	59.3 (26.7)	<i>2.0 (0.9)</i>	<i>7.0 (3.1)</i>	
30%-<40%		<b>14.6 (6.6)</b>	29.5 (13.2)	<i>2.7 (1.2)</i>	
40%-			<b>11.9 (5.3)</b>	35.7 (16.0)	
Total					222.3 (100.0)
Expected Number in Events*, <i>n</i> (%)					
<20%	2.3 (2.1)	<b>0.0 (0.0)</b>	<b>1.0 (0.9)</b>		
20%-<30%	<i>1.0 (0.9)</i>	21.7 (19.2)	<b>2.0 (1.8)</b>	<b>4.0 (3.5)</b>	
30%-<40%		<i>4.4 (3.9)</i>	26.5 (23.6)	<b>2.3 (2.1)</b>	
40%-			<i>7.1 (6.3)</i>	40.3 (35.8)	
Total					112.7 (100.0)

**Bold numbers** indicate improved reclassifications, while *Italicized numbers* indicate worsened reclassifications by adding non-calprit CT-HRP to the Model 2.

\* Expected numbers were calculated by the Kaplan-Meier method in subgroups defined by the combination of the predicted risk-categories from Model 2 and Model 3.