

DATA SUPPLEMENT

Prognostic Value of Estimated Functional Capacity Incremental to Cardiac Biomarkers in Stable Cardiac Patients

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Supplement 1: Nomogram Development

A built-in function in the statistical R package, `nomogram`, was used to construct the nomogram¹⁻³. Absolute beta values are ranked based on the estimated regression coefficients. First step is to determine which predictor has the biggest impact in the model. Then, the next step is to sequentially assign scores to other predictors based on their proportions to the point assigned to the most important predictor. Estimated beta coefficients from a Cox model were used as followed:

Predictor	Level	Beta	Values	Absolute maximum beta value	Rank	
Age	Unit=1	0.0381	10 to 100 by 10	$0.0381 \times (100 - 10) = 3.429$	1	100 assigned to age=100; 0 assigned to age=10; Assign points to other age values based on the linear interpolation
HDL	Unit=1	-0.0063	0 to 180 by 20	$0.0063 \times (180 - 0) = 1.134$	2	$100 \times (1.134 / 3.429) = 33$ assigned to HDL=0; 0 assigned to HDL=180; Assign points to other HDL values based on the linear interpolation
Smoking	1	0.2368	0, 1	0.2368	3	$100 \times (0.2368 / 3.429) = 7$ assigned to smokers
Gender	Male	-0.0499	Female, Male	0.050	4	$100 \times (0.05 / 3.429) = 1$ assigned to female

The Cox model used age, gender, HDL, and smoking as predictors. Steps of assigning scores to each predictor are shown below.

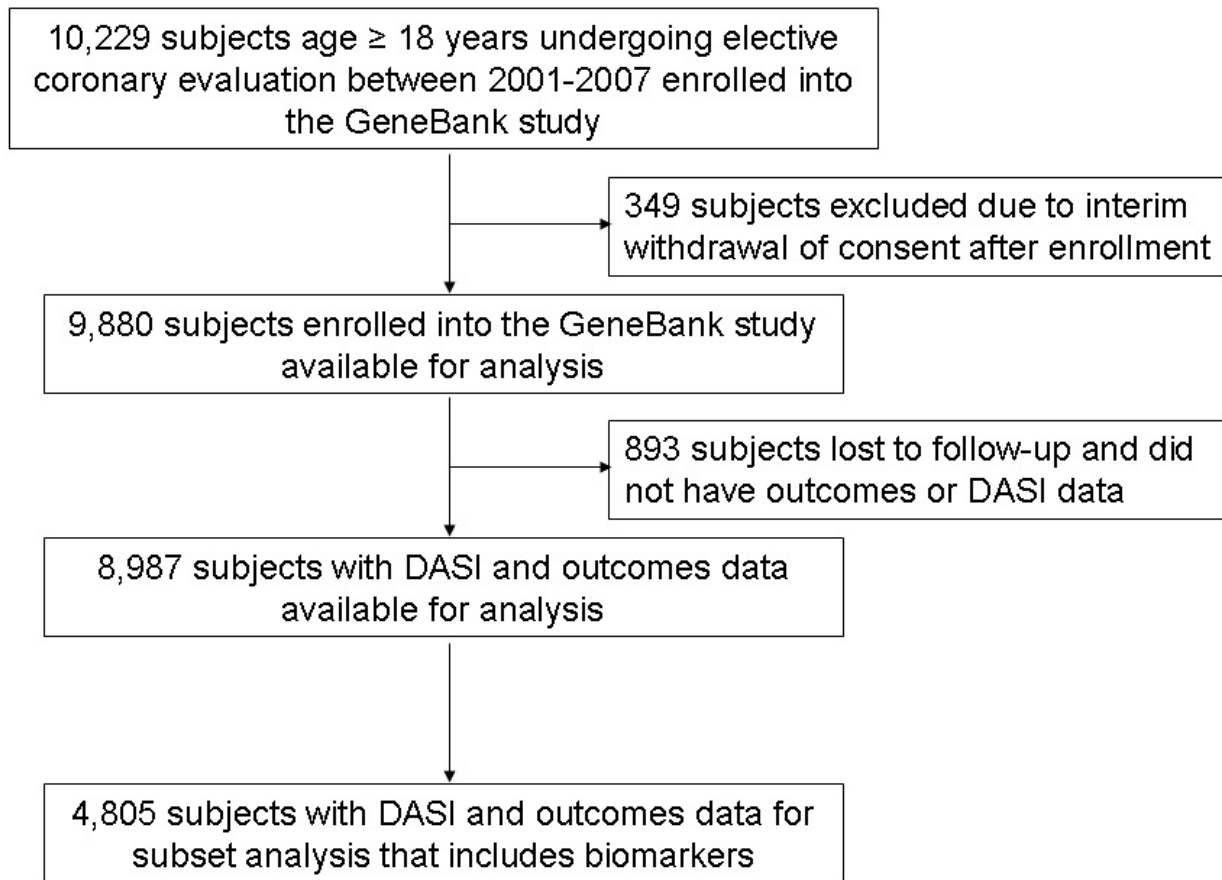
- 1) Age (Continuous variable): The range of age values is chosen to be the minimum and maximum values that will be displayed on the nomogram, which is 0 and 100 in this case. The calculated absolute maximum beta value= $0.0381(100-10)=3.429$. In comparison to the maximum beta value of Gender (0.05), HDL (1.134), and smoking (0.2368), age has the biggest impact on the risk of the event. So we assign 100 to age=100, and 0 to age=0 and points to other age values based on the linear interpolation.
- 2) Gender (categorical variable with two levels): The total point of the factor gender is assigned based on its proportion to the total point of the age=100 (point=100). The formula is: Total point of male = $100 \times (\text{absolute maximum beta value for gender} / \text{absolute maximum beta value for age}) = 100 \times (0.05 / 3.429) = 1$
So a male patient is assigned 1 point, whereas 0 for a female patient.

- 3) HDL (continuous variable): The range for HDL is from 0 to 180. The total point assigned to HDL is $100 \times (1.134/3.429) = 33$. So 33 is assigned to HDL=0 and 0 assigned to HDL=180 and points assigned to other HDL values based on the linear interpolation.

Reference:

- 1) Harrell FE. Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis (Springer Series in Statistics). Springer, New York, NY, 2001.
- 2) Harrell FE. rms: Regression Modeling Strategies. R package version 3.6-3, 2013.
- 3) Iasonos A1, Schrag D, Raj GV, Panageas KS. How to build and interpret a nomogram for cancer prognosis. J Clin Oncol. 2008;26:1364-1370.

Supplement 2: CONSORT Diagram



Supplement 3: Unadjusted and adjusted Hazard ratio (HR) for Major Adverse Cardiac Events at 3 years According to Canadian Cardiovascular Society (CCS) Angina Class

	Quartile 4	Quartile 3	Quartile 2	Quartile 1
CCS Class 0 (n=231)				
<i>Range</i>	≥51	42-51	25-42	<25
Unadjusted HR	1	1.48 (0.49-4.51)	2.34 (0.97-5.64)	3.13 (1.32-7.40)**
Adjusted HR	1	1.32 (0.43-4.03)	2.4 (0.93-6.15)	3.22 (1.26-8.22)*
Event rate	9.9%	14.3%	22.4%	28.1%
CCS Class I (n=2,827)				
<i>Range</i>	≥51	43-51	27-43	<27
Unadjusted HR	1	1.80 (1.22-2.65)**	2.99 (2.19-4.08)***	5.55 (4.20-7.35)***
Adjusted HR	1	1.63 (1.09-2.42)*	2.62 (1.89-3.62)***	4.60 (3.35-6.31)***
Event rate	5.8%	10.4%	16.7%	28.9%
CCS Class II (n=2,102)				
<i>Range</i>	≥51	39-51	27-39	<27
Unadjusted HR	1	1.93 (1.25-2.99)**	1.99 (1.33-2.99)***	4.59 (3.19-6.60)***
Adjusted HR	1	1.75(1.13-2.72)*	1.66(1.10-2.51)*	3.68 (2.52-5.38)***
Event rate	5.7%	11.0%	11.4%	23.9%

CCS Class III (n=1,178)				
<i>Range</i>	≥46	34-46	19-34	<19
Unadjusted HR	1	0.81 (0.48-1.38)	2.13 (1.38-3.27) ^{***}	2.97 (1.94-4.55) ^{***}
Adjusted HR	1	0.71 (0.42-1.21)	1.64 (1.04-2.60) [*]	2.15 (1.33-3.47) ^{**}
Event rate	10.1%	8.5%	20.6%	26.5%
CCS Class IV (n=2,176)				
<i>Range</i>	≥51	35-51	21-35	<21
Unadjusted HR	1	2.39 (1.63-3.50) ^{***}	2.50 (1.66-3.76) ^{***}	5.06 (3.55-7.20) ^{***}
Adjusted HR	1	2.11 (1.43-3.09) ^{***}	2.10 (1.38-3.18) ^{***}	4.01 (2.74-5.86) ^{***}
Event rate	6.0%	13.8%	14.3%	26.9%

Adjusted for traditional risk factors include age, gender, systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, smoking, diabetes mellitus. * p<0.05; **p<0.01; ***p<0.001