RESEARCH ARTICLE

Which Biology Marker Can be a Predictor for Higher Syntax Score?

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Abstract

BACKGROUND: Syntax score is a lesion-based angiographic scoring system, originally devised to grade the anatomic complexity of coronary artery disease (CAD) and thereby facilitate consensus in the study of a diagnostic angiogram between surgeons and interventional cardiologists. Suitable biology marker to predict the severity of CAD and to have a treatment decision for revascularisation by percutaneous coronary intervention (PCI) or bypass surgery, is still unknown. Which biology marker can be a predictor for higher Syntax score remains unknown as well.

METHODS: Severity of 105 patients who underwent coronary angiography, were evaluated with Syntax score. Laboratory tests were conducted for routine blood test, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), high-sensitivity C-reactive protein (hs-CRP), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, kidney function, creatinine and hemoglobin A1c (HbA1c).

RESULTS: Ureum had significant correlation with Syntax score, p=0.016 and 95% confidence interval (CI): 0.05-0.55. Result of logistic regression analysis showed that HDL and haematocrit had significant correlation with Syntax score, with cut off point 34 (p=0.02, p=0.0033, respectively).

Abstrak

LATAR BELAKANG: Skor *Syntax* adalah sistem skor angiografi yang menentukan keparahan penyakit jantung koroner (PJK) secara anatomi, sehingga memfasilitasi konsensus studi angiogram diagnostik antara ahli bedah dan kardiologis intervensional. Marker biologis yang tepat dalam hal memperkirakan keparahan PJK dan menentukan pengobatan revaskularisasi dengan tindakan dilatasi dengan balon dan pemasangan *stent* atau operasi *bypass*, belum diketahui. Biologi marker mana yang bermanfaat dalam penentuan skor *Syntax* yang tinggi, juga belum diketahui.

METODE: Keparahan dari 105 pasien yang menjalani angiografi koroner, dievaluasi dengan perhitungan skor *Syntax*. Pemeriksaan laboratorium yang dilakukan adalah pemeriksaan darah rutin, *high-sensitivity C-reactive protein* (hs-CRP), total kolesterol, kolesterol *low-density lipoprotein* (LDL), kolesterol *high-density lipoprotein* (HDL), trigliserida, fungsi ginjal, kreatinin dan hemoglobin A1c (HbA1C).

HASIL: Ureum berkorelasi signifikan dengan skor *Syntax,* p=0.016 dan 95% *confidence interval* (CI): 0.05-0.55. Hasil analisa regresi logistik memperlihatkan HDL dan hematokrit berkorelasi signifikan dengan skor *Syntax,* dengan *cut off point* 34 (p=0.02, p=0.0033, secara berurutan). Berdasarkan

Based on multi-variate analysis, Syntax score 34 = 16 (HDL ≤40 + Ureum ≥23) + 10 (Neutrophil/Lymphocyte ≥3.789) +10 (HbA1c ≥7) + 13 (monocyte ≥9%).

CONCLUSION: HDL cholesterol, ureum, neutrophil-lymphocyte ratio, HbA1c and monocyte altogether can predict the higher Syntax score.

KEYWORDS: syntax, neutrophil, lymphocyte, HDL, cholesterol, ureum, HbA1c, monocyte

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analisa multivariat, skor Syntax 34 = 16 (HDL ≤40 + Ureum ≥23) + 10 (Neutrofil/Limfosit ≥3.789) +10 (HbA1c ≥7) + 13 (monosit ≥9%).

KESIMPULAN: Kolesterol HDL, ureum, rasio neutrofil-limfosit, HbA1C dan monosit secara bersama dapat menentukan skor *Syntax* yang tinggi.

KATA KUNCI: *syntax*, netrofil, limfosit, HDL, kolesterol, ureum, HbA1c, monosit

Introduction

Coronary artery disease (CAD) is a disease pertaining to plaque atherosclerosis which could tighten as well as block the blood vessel of artery coronary (1-3). Myocardium will not have enough blood supply as well as oxygen for myocardium contraction, leading to ischemic, heart attack and mortality. To prevent this, revascularization will be needed either with percutaneous coronary intervention (PCI) or bypass surgery, depending on the severity of coronary disease.

Syntax score is a lesion-based angiographic scoring system, originally devised to grade the anatomic complexity of CAD and thereby facilitate consensus in the study of a diagnostic angiogram between surgeons and interventional cardiologists.(1,2) Suitable biology marker to predict the severity of CAD and to have a treatment decision for revascularization by percutaneous coronary intervention (PCI) or bypass surgery, is still unknown.(4-8)

Methods

Subjects Recruitment and Selection

Subjects were recruited from Medistra hospital who underwent coronary angiography. Patients with infectious diseases, severe liver, renal disease and revascularization history, were excluded. Upon explanation, all subjects had to sign written informed consent. This study was approved by Ethics Committee of Faculty of Medicine, Hasanuddin University.

Subjects Examination and Calculation of Syntax Score

Subjects enrolled in this study underwent detailed clinical and angiographic examinations. Subjects were asked for their medical history, smoking habit, hypertension, diabetes mellitus, hypercholesterolemia and family medical history. Calculation of Syntax score was conducted with online spplication at www.syntaxscore.com/calculation.(5)

Laboratory Test

Blood samples were collected in the morning after overnight fasting for 12 hours. Routine blood test was performed, and serum was separated not more than 2 hours after blood collection. Serum levels of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), ureum, creatinine, high-sensitivity C-reactive protein (hs-CRP), total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol and triglyceride were assayed using auto-analyser Cobas (Roche Diagnostics, Indianapolis, IN, USA).

Statistical Analysis

Statistical Analysis were performed using Strata (College Station, Tx, USA). Regression linear, logistic regression and multivariate tests were conducted with significant level at $p<0.05$.

Results

Total 105 patients were enrolled in this study from January to December 2013, only 16 patients (15%) had asymptomatic angina. Syntax score >34 were 27 patients (25.7%). Patients with hypertension and diabetes mellitus had higher Syntax score than patients without history of hypertension and diabetes mellitus, but not significant (hypertension, $p=0.227$; diabetes mellitus, $p=0.386$).

Regression linear analysis in Table 2 showed that only ureum had significant correlation with Syntax score, $p=0.016$ and 95% confidence interval (CI): 0.05-0.55. We

Table 1. Distribution of variables.

No.	Variable	Mean	SEM*	Min	Max
1	Age (year old)	57.6	0.97	33	78
2	high (cm)	166.58	0.85	145	185
3	Body weight (kg)	73.44	1.32	47	125
4	Body mass index	26.4	0.39	18.82	41.76
5	Body surface area (m^2)	1.81	0.02	1.39	2.36
6	Haemoglobin (mg/dL)	14.05	0.15	9.8	17.4
7	Haematocrit (%)	41.02	0.51	11.7	52
8	Leukocyte	10.85	2.44	2.16	262
9	Thrombocyte	249.13	5.64	134	526
10	Basophil (%)	552381	0.12	0	9
11	Eosinophil (%)	2.72	0.25	0	11
12	Band neutrophil (%)	0.29	0.1	0	5
13	Segmented neutrophil (%)	62.98	0.97	43	89
14	Lymphocyte (%)	26.44	0.83	7	47
15	Monocyte (%)	7.36	0.38	0	38
16	Total cholesterol (mg/dL)	193.62	4.34	105	324
17	HDL (mg/dL)	44.94	1.68	25	183
18	LDL (mg/dL)	121.31	1.06	28	292
19	Triglyceride (mg/dL)	155.31	6.65	39	405
20	Ureum (mg/dL)	26.8	0.97	9	74
21	Creatinine (mg/dL)	0.94	0.02	0.04	1.6
22	Uric acid (mg/dL)	6.28	0.23	2.9	24
23	SGOT (U/L)	24.49	1.49	7	152
24	SGPT (U/L)	27.56	1.54	6	104
25	Fasting blood sugar (mg/dL)	107.99	3.41	28	352
26	LV-EF (%)	56.5	1.03	22	78
27	HbA1c (%)	6.81	0.1	4.8	10.1
28	hs-CRP (mg/L)	7.51	1.79	0.1	119
29	Syntax Score	23.77	1.25	3	62

*SEM: Standard Error Mean (Standard Deviation/√n)

Table 2. Regression linear test for Syntax scorewith cut off point 34.

No.	Variable	*F*	*R2*	*t*	*p**	95% CI
1	Total cholesterol	0.17	0.0016	-0.41	0.685	(-0.81; 0.53)
2	LDL cholesterol	0	0	0.01	0.991	(-0.06; 0.06)
3	HDL cholesterol	0.69	0.0066	-0.83	0.409	(-0.206; 0.084)
4	Creatinin	0.18	0.0017	0.42	0.676	(-8.56; 13.15)
5	Ureum	5.94	0.0545	2.44	**0.016**	(0.05; 0.55)
6	hs-CRP	0.18	0.0017	-0.42	0.672	(-0.16; 0.107)
7	SGOT	0.61	0.0059	-0.78	0.436	(-0.22; 0.09)
8	SGPT	1.22	0.0117	-1.1	0.272	(-0.246; 0.07)
9	Body mass index	1.31	0.0125	-1.14	0.255	(-0.978; 0.262)
10	Neutrophil-lymphocyte ratio	0.25	0.0024	0.5	0.619	(-0.02; 3.61)

*Regression Linear test

Table 3. Logistic Regression test for Syntax score with cut off point 34.

No.	Variable	*p*	Odd Ratio	95% CI
1	Total cholesterol	0.927	1.0004	0.99; 1.01
2	LDL cholesterol	0.35	1.005	0.99; 1.015
3	HDL cholesterol	0.02	0.936	0.885; 0.989
4	Left ventricle ejection fraction	0.243	0.975	0.93; 1.01
5	hs-CRP (impute)	0.957	1.009	0.72; 1.41
6	Creatinine	0.255	0.327	0.048; 2.23
7	Ureum (impute)	0.092	1.038	0.99; 1.08
8	Hypertension	0.598	1.26	0.52; 3.04
9	Age	0.324	1.02	0.97; 1.07
10	Hypercholesterolemia	0.523	0.657	0.18; 2.38
11	Smoker	0.412	1.51	0.56; 4.04
12	Diabetes Mellitus	0.248	1.696	0.69; 4.15
13	Family history	0.662	1.48	0.255; 8.57
14	Triglyceride (impute)	0.961	0.975	0.36; 2.63
15	Body mass index	0.311	0.94	0.83; 1.05
16	Neutrophil-lymphocyte ratio	0.214	1.13	0.93; 1.38
17	Basophil	0.147	0.173	0.016; 1.84
18	Haemoglobin	0.072	0.76	0.57; 1.02
19	Haematocrit	0.033	0.903	0.82; 0.99
20	Leukocyte	0.248	1.07	0.95; 1.21
21	Thrombocyte	0.329	1.003	0.99; 1.01
22	Eosinophil	0.576	0.95	0.79; 1.13
23	Band neutrophil	0.654	1.09	0.73; 1.65
24	Segmented neutrophil	0.437	1.01	0.97; 1.06
25	Lymphocyte	0.295	0.97	0.92; 1.02
26	Monocyte	0.235	1.07	0.95; 1.19
27	Uric acid	0.434	0.91	0.72; 1.15
28	SGOT	0.65	0.99	0.95; 1.02
29	SGPT	0.989	1.0001	0.97; 1.02
30	Fasting blood sugar	0.401	1.005	0.99; 1.01
31	HbA1c	0.053	1.51	0.99; 2.3
32	Chest pain	0.541	1.31	0.54; 3.17

Table 4. Multivariate predictor Syntax Score >34.

Variable	Cut Off	*p*	Odd Ratio	Coefficients	*z*	Score
HDL	≤40	0.062	2.51	0.9225703	1.87	35
Ureum	≥23	0.021	4.15	1.423749	2.31	43
Neutrophil/ lymphocyte	≥3.789	0.186	2.24	0.805509	1.32	25
HbA1c	≥7	0.598	1.32	0.2834972	0.53	10
Monocyte	≥9%	0.116	2.31	0.8379034	1.57	29

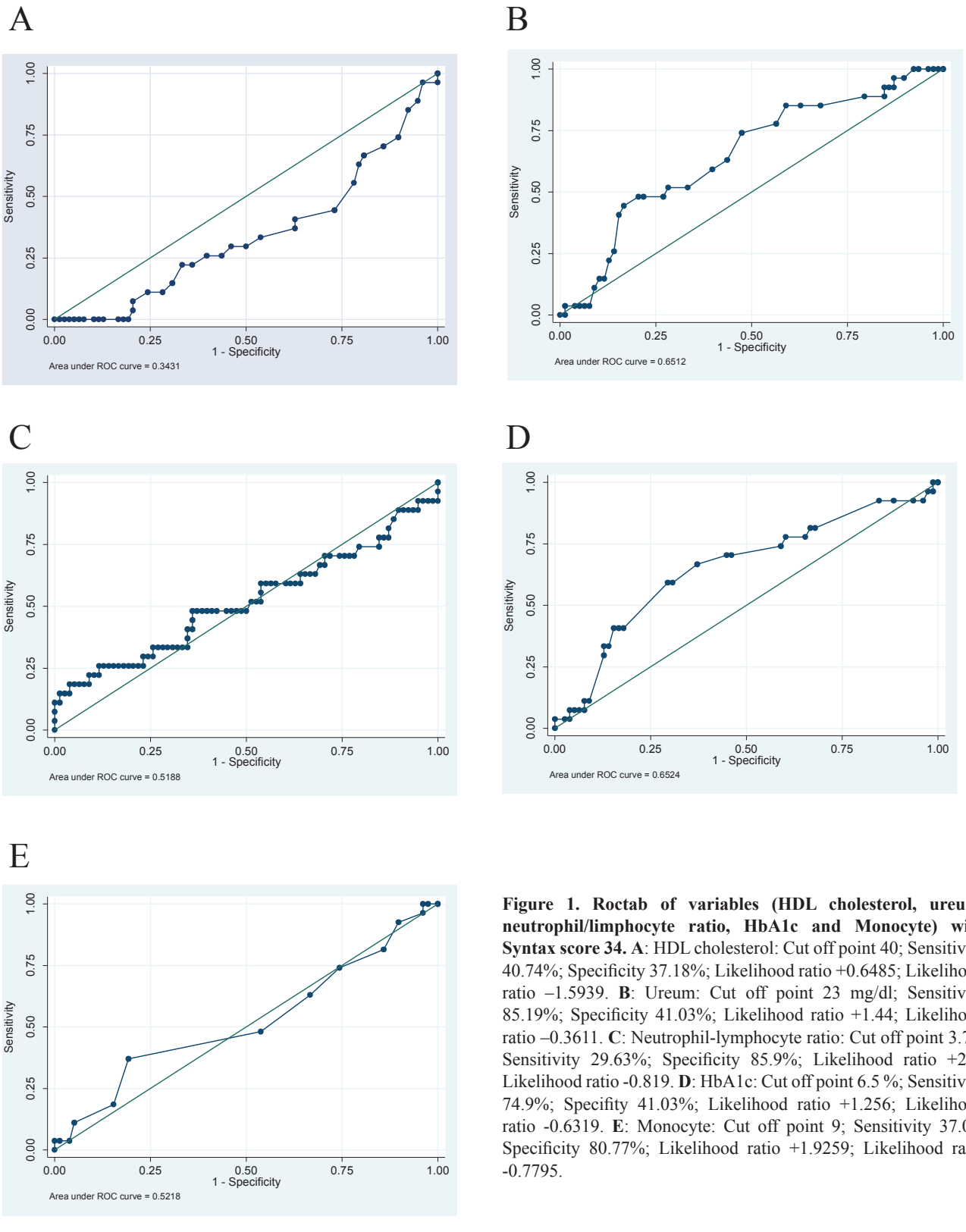

Figure 1. Roctab of variables (HDL cholesterol, ureum, neutrophil/limphocyte ratio, HbA1c and Monocyte) with Syntax score 34. A: HDL cholesterol: Cut off point 40; Sensitivity 40.74%; Specificity 37.18%; Likelihood ratio +0.6485; Likelihood ratio –1.5939. **B**: Ureum: Cut off point 23 mg/dl; Sensitivity 85.19%; Specificity 41.03%; Likelihood ratio +1.44; Likelihood ratio –0.3611. **C**: Neutrophil-lymphocyte ratio: Cut off point 3.79; Sensitivity 29.63%; Specificity 85.9%; Likelihood ratio +2.1; Likelihood ratio -0.819. **D**: HbA1c: Cut off point 6.5 %; Sensitivity 74.9%; Specifity 41.03%; Likelihood ratio +1.256; Likelihood ratio -0.6319. **E**: Monocyte: Cut off point 9; Sensitivity 37.04; Specificity 80.77%; Likelihood ratio +1.9259; Likelihood ratio -0.7795.

used Syntax Score 34 as cut off point as reported previously. (9)

Result of logistic regression analysis showed that HDL and haematocrit had significant correlation with Syntax score with cut off point 34 (p=0.02, p=0.0033, respectively) (Table 3).

Based on multi-variate analysis, Syntax score 34 = 16 (HDL ≤40 + Ureum ≥23) + 10 (Neutrophil/Lymphocyte ≥3.789) +10 (HbA1c ≥7) + 13 (monocyte ≥9%).

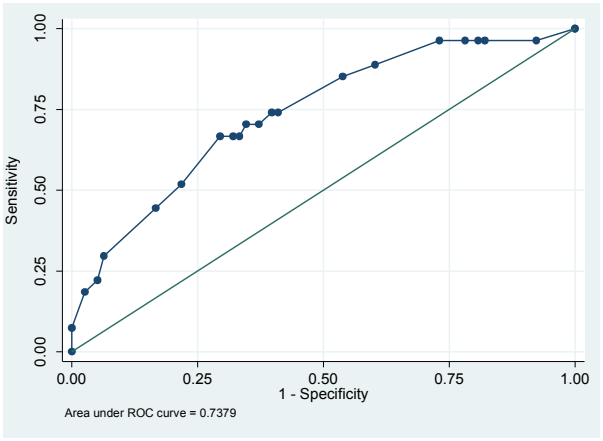

Figure 2. Roctab scoring to predict Syntax score >34. Score model can predict 73.53%; Cut off point 70; Sensitivity 70.37%; Specificity 65.38%; Likelihood ratio +2.0329; Likelihood ratio –0.4532; Risk 67%.

Discussion

Based on our current result, we found that there was not a significant correlation between neutrophil-lymphocyte ratio and Syntax score. This could be related to the ongoing treatment performed to our subjects, such as antiplatelet, aspirin, clopidogrel, also statins that decrease lipid level.

For neutrophil-lymphocyte ratio, different with our results, other reports (10-17) showed that acute coronary syndrome patients with ST elevation nor without ST elevation, will have neutrophil-lymphocyte ratio as an independent factor for the mortality(18-20). In accordance to our results, Arbel *et al*. reported patients with >3 neutrophil-lymphocyte ratio, will have more severity than the patients with ratio <3.(20) In our study, only 30% subject with angina pectoris class III and 20% angina pectoris class IV.

In our study, we found that history of hypertension and diabetic mellitus were positively correlated with syntax score. Although the correlation was not significant, but relative higher in patient with syntax score ≥34. Therefore patients with the history of hypertension and diabetic mellitus, will have higher syntax scores. These results are in accordance to reports showing that hypertension and diabetes mellitus are risk factors. Eventually the risks can induce dysfunction of coronary arteries endothelium and activate LDL cholesterol in the blood vessel wall, leading to plaque formation, then tightness and blockage of coronary arteries will be occured (1,21-23). In our results, there was no correlation between Syntax score and hypercholesterolemia, since our patients has already been treated with lipid reducing medicine. We are awared that there are limitations in our study, therefore further research should be pursued, especially in functional Fractional Flow Reserve (FFR), Euro Score and Syntax score II (24).

Conclusion

Marker biology of HDL cholesterol, Ureum, neutrophil/lymphocyte ratio, HbA1c and Monocyte together will be predictor of higher syntax score.

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