

Association of Calculated Serum Osmolality with High-complexity Coronary Lesions: Insights from the SYNTAX Score

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Abstract

Objective: The SYNTAX score quantifies coronary lesion complexity and guides revascularization in coronary artery disease (CAD). Readily available biomarkers that reflect lesion burden may improve preangiography risk stratification. This study evaluated whether calculated serum osmolality is associated with lesion complexity in stable CAD.

Methods: Adults undergoing elective coronary angiography between January and December 2023 were retrospectively analyzed. Serum osmolality was calculated as $2 \times [\text{Na}^+] + [\text{BUN}/2.8] + [\text{Glucose}/18]$. Patients were classified as having a low (≤ 22) or moderate-high (> 22) SYNTAX score. Variables identified by least absolute shrinkage and selection operator (LASSO) regression were tested in multivariable logistic regression.

Results: A total of 281 patients were included; 195 (69.4%) had a low SYNTAX score, and 86 (30.6%) had a moderate-high SYNTAX score. Median osmolality was significantly higher in the moderate-high group than in the low-score group (293.2 vs. 288.1 mOsm/kg; $p < 0.001$). In multivariable analysis, serum osmolality was the strongest independent predictor of a high SYNTAX score (OR, 1.123; 95% CI, 1.070–1.184; $p < 0.001$), along with age, chronic obstructive pulmonary disease, and lipid parameters. Receiver operating characteristic analysis revealed an area under the curve of 0.75 (95% CI, 0.69–0.81).

Conclusion: Calculated serum osmolality, a simple and universally available parameter, is independently associated with angiographic lesion complexity in stable CAD and may contribute to preangiography risk stratification and revascularization planning.

Keywords: Coronary artery disease; serum osmolality; SYNTAX score.

Hesaplanmış Serum Osmolalitesinin Yüksek Karmaşıklıkta Koroner Lezyonlarla İlişkisi: SYNTAX Skoruna Dayalı Bulgular

Özet

Amaç: SYNTAX skoru, koroner lezyon kompleksitesini nicel olarak belirleyerek revaskülarizasyon stratejilerini yönlendirmekte ve koroner arter hastalığında (KAH) prognozu öngörmektedir. Lezyon yükünü yansıtan, kolay ulaşılabilir biyobelirteçler anjiyografi öncesi risk sınıflamasını güçlendirebilir. Bu çalışmada, hesaplanmış serum osmolalitesinin stabil KAH hastalarında SYNTAX skoru ile bağımsız olarak ilişkili olup olmadığı değerlendirildi.

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Yöntem: Ocak–Aralık 2023 tarihleri arasında elektif koroner anjiyografi yapılan ardışık erişkin hastalar retrospektif olarak incelendi. Serum osmolalitesi, $2 \times [\text{Na}^+ (\text{mmol/L})] + [\text{BUN} (\text{mg/dL})/2.8] + [\text{glukoz} (\text{mg/dL})/18]$ formülü ile hesaplandı. Hastalar, SYNTAX skoru ≤ 22 olanlar (düşük) ve > 22 olanlar (orta–yüksek) şeklinde gruplandırıldı. Tek değişkenli analizde $p < 0,10$ bulunan değişkenler LASSO lojistik regresyona dâhil edildi; λ min’de sıfır olmayan katsayıya sahip değişkenler çok değişkenli lojistik regresyona alındı. Nomogram oluşturuldu ve bootstrap yöntemiyle doğrulaması yapıldı.

Bulgular: Çalışmaya 281 hasta dâhil edildi; bunların 195’i (%69,4) düşük, 86’sı (%30,6) orta–yüksek SYNTAX skoruna sahipti. Orta–yüksek grubun medyan osmolalitesi daha yüksek saptandı (293,2 vs. 288,1 mOsm/kg; $p < 0,001$). Çok değişkenli analizde serum osmolalitesi, yüksek SYNTAX skorunun bağımsız bir öngördürücüsüydü (OR 1,123; %95 CI 1,070–1,184; $p < 0,001$). Ayrıca yaş, KOAH, HDL ve LDL kolesterolün de anlamlı olduğu saptandı. ROC analizinde AUC 0,75 olarak bulundu (%95 CI 0,69–0,81).

Sonuç: Rutin laboratuvar testlerinden elde edilebilen, basit ve düşük maliyetli bir parametre olan hesaplanmış serum osmolalitesi, stabil KAH’da anjiyografik lezyon kompleksitesi ile bağımsız olarak ilişkilidir. Bu belirtecin anjiyografi öncesi değerlendirmeye eklenmesi, bireyselleştirilmiş revaskülarizasyon stratejilerinin planlanmasına ve risk sınıflamasına katkıda bulunma potansiyeline sahip olabilir.

Anahtar sözcükler: Koroner arter hastalığı; serum osmolalitesi; SYNTAX skoru.

Introduction

Coronary artery disease (CAD) remains a major global cause of morbidity and mortality, and complex coronary anatomy poses particular challenges for revascularization strategies and long-term outcomes.^[1] The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score is a validated angiographic tool that quantifies lesion complexity, predicts adverse cardiovascular events, and guides decision-making between percutaneous coronary intervention and coronary artery bypass grafting.^[2] It is derived from coronary angiography by assessing the full extent of the major coronary arterial tree and incorporating coronary dominance into the calculation. Identifying readily available biomarkers that correlate with the SYNTAX score may enhance risk stratification and support personalized treatment planning.^[2,3]

Serum osmolality, a calculated parameter reflecting the combined osmotic load of sodium, glucose, and blood urea nitrogen, has traditionally been used to assess fluid and electrolyte disturbances.^[4] Even mild elevations in osmolality may reflect systemic hemodynamic and inflammatory changes that contribute to atherosclerotic burden and lesion complexity.^[4,5] Because serum osmolality is simple and cost-effective to calculate, investigating its potential utility for early risk stratification in atherosclerosis and for guiding timely preventive interventions is of considerable clinical relevance.

To our knowledge, no study has comprehensively examined the association between calculated serum osmolality and angiographic lesion complexity as measured by the SYNTAX score.^[2,3] In this retrospective analysis, we aimed to determine whether calculated serum osmolality independently predicts higher SYNTAX scores in patients undergoing elective coronary angiography.

Materials and Methods

Study Design and Population

This retrospective study was conducted at a tertiary care center between January and December 2023. Consecutive patients who underwent elective coronary angiography were screened according to predefined inclusion and exclusion cri-

teria. A total of 281 patients met the study criteria and were included in the analysis. The inclusion criteria were as follows: age ≥ 18 years; de novo coronary artery disease, defined as $\geq 50\%$ stenosis in at least one epicardial coronary artery on angiography; and availability of fasting laboratory measurements obtained on the same day as angiography. The exclusion criteria were acute coronary syndrome (ST-elevation myocardial infarction [MI], non-ST-elevation MI, or unstable angina pectoris); prior history of CAD or revascularization; end-stage renal disease [estimated glomerular filtration rate (eGFR) $< 30 \text{ mL/min/1.73m}^2$]; diabetes mellitus; use of medications known to affect serum osmolality (e.g., mannitol and diuretics); and incomplete or missing clinical or laboratory data. Serum osmolality (mOsm/kg) was calculated for all participants using the standard formula: $2 \times [\text{Na}^+ (\text{mmol/L})] + [\text{BUN} (\text{mg/dL})/2.8] + [\text{Glucose} (\text{mg/dL})/18]$. All biochemical parameters, including sodium, blood urea nitrogen, glucose, lipid profile, and complete blood count, were obtained from fasting venous blood samples collected before coronary angiography. Coronary angiographic procedures were performed using a Siemens Artis floor-based angiography system (Siemens, Germany). Patients were stratified into two groups according to SYNTAX score: low risk (SYNTAX ≤ 22) and moderate-to-high risk (SYNTAX > 22). The SYNTAX score was calculated using the official online calculator and was independently assessed by two senior interventional cardiologists.^[6] eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) study formula.^[7] Hypertension was defined as a documented medical diagnosis or the presence of elevated blood pressure values, specifically systolic blood pressure $> 140 \text{ mmHg}$ or diastolic blood pressure $> 90 \text{ mmHg}$. All participants underwent transthoracic echocardiographic assessment within the first 24 hours after the procedure using a Philips Epiq 7 system (Philips Medical Systems, Andover, MA, USA). The study protocol complied with the principles of the Declaration of Helsinki and was approved by the Izmir Katip Çelebi University Health Research Ethics Committee (Approval Number: 0473, Date: 17.07.2025). Because the study was retrospective, the requirement for informed consent to participate was waived by the Institutional Review Board.

Statistical Analysis

Statistical analyses were performed using Jamovi (version 2.4.8; The Jamovi Project, Sydney, Australia) and R software (version 4.4.0; R Foundation for Statistical Computing, Vienna, Austria). Because continuous variables were not normally distributed, they were presented as medians with interquartile ranges, and group differences were analyzed using the Mann–Whitney U test. Categorical variables were expressed as counts and percentages and were compared using the chi-square or Fisher’s exact test, as appropriate.

Variables with a p-value<0.10 in univariate analysis were considered potential predictors and were included in the least absolute shrinkage and selection operator (LASSO) logistic regression model for variable selection. LASSO regression was performed using 10-fold cross-validation to determine the optimal regularization parameter (lambda.min), and variables with nonzero coefficients at this threshold were selected for multivariable logistic regression.

The discriminatory performance of serum osmolality was evaluated using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated with 95% confidence intervals (CI) using the DeLong method. The optimal cutoff value was determined using the Youden index. A nomogram was constructed based on the final multivariable model, and model calibration was assessed using 1000 bootstrap resamples. A two-tailed p-value<0.05 was considered statistically significant.

Results

A total of 281 patients who underwent elective coronary angiography between January and December 2023 were included in the analysis. Among them, 195 (69.4%) had a SYNTAX score≤22, and 86 (30.6%) had a SYNTAX score>22. Baseline characteristics are summarized in Table 1. Compared with the low-SYNTAX group, patients with a high SYNTAX score were more often male (93% vs. 76.4%, p<0.001) and had a higher prevalence of chronic obstructive pulmonary disease (COPD) (14% vs. 5.1%, p=0.011). The prevalence of hypertension and left ventricular ejection fraction (LVEF) did not differ significantly between groups.

Laboratory results are presented in Table 2. Compared with the low-SYNTAX score group, patients with a SYNTAX score>22 had higher median serum glucose (116 vs. 101mg/dL; p<0.001), sodium (141 vs. 139mmol/L; p<0.001), low-density lipoprotein (LDL) cholesterol (143 vs. 131mg/dL; p=0.047), and calculated serum osmolality (293.2 vs. 288.1mOsm/kg; p<0.001), whereas high-density lipoprotein (HDL) cholesterol levels were lower (39 vs. 43mg/dL; p=0.009). Variables with p<0.10 in univariate analysis were entered into LASSO regression (Fig. 1a, b), which identified seven variables with nonzero coefficients at λ_{min}—age, sex, smoking, COPD, HDL, LDL, and serum osmolality—for inclusion in multivariable analysis.

In the adjusted model (Table 3), serum osmolality remained the strongest independent predictor of a high SYNTAX score (OR, 1.123 per mOsm/kg; 95% CI, 1.070–1.184; p<0.001). Other significant predictors were age (OR, 1.038 per year; 95% CI, 1.003–1.076; p=0.037), COPD (OR, 3.145; 95% CI, 1.035–10.106; p=0.047), HDL (OR, 0.952 per mg/dL; 95% CI, 0.922–0.980; p=0.001), and LDL (OR, 1.013 per mg/dL; 95% CI, 1.004–1.022; p=0.004). Smoking showed a borderline association (OR, 1.793; 95% CI, 0.958–3.406; p=0.070), whereas sex was not statistically significant. The adjusted effect of serum osmolality on the probability of a SYNTAX score>22 is illustrated in Figure 2, showing a steady increase in predicted risk with increasing osmolality. Receiver operating characteristic (ROC) analysis for osmolality alone (Fig. 3) demonstrated fair discrimination (AUC, 0.717; 95% CI, 0.648–0.787; p<0.001), with an optimal cutoff value of 291.6mOsm/kg. A nomogram incorporating all seven predictors was constructed to facilitate clinical application (Fig. 4), and calibration analysis with 1000 bootstrap resamples confirmed excellent agreement between predicted and observed probabilities (Fig. 5), with the bias-corrected curve closely following the 45° line.

Discussion

Our findings suggest, for the first time, that calculated serum osmolality is independently associated with angiographic lesion complexity as quantified by the SYNTAX score. In contrast to previous studies, which have primarily examined acute coronary

Table 1. Baseline characteristics stratified by SYNTAX score category

Variables	Overall n=281		Low SYNTAX score (≤22) n=195		Moderate-high SYNTAX score (>22) n=86		p
	n	%	n	%	n	%	
Age (years)	65 (57–70)		63 (57–69)		66 (56.8–72.8)		0.085
Male sex	229	81.5	149	76.4	80	93.0	<0.001
LVEF (%)	60 (55–60)		60 (55–60)		60 (52–60)		0.301
Hypertension	171	60.9	123	63.1	48	55.8	0.250
COPD	22	7.8	10	5.1	12	14.0	0.011
Smoking	134	47.7	86	44.1	48	55.8	0.070
SYNTAX score	12 (7–24)		10 (6–13)		29 (25–37)		<0.001
Atrial fibrillation	16	5.7	10	5.1	6	7.0	0.538

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; LVEF: Left ventricular ejection fraction; COPD: chronic obstructive pulmonary disease.

Table 2. Laboratory findings stratified by SYNTAX score category

Variables	Overall n=281	Low SYNTAX score (≤ 22) n=195	Moderate-high SYNTAX score (>22) n=86	p
WBC ($10^9/L$)	8.05 (6.87–9.38)	8.0 (6.9–9.3)	8.1 (7.0–9.5)	0.438
Neutrophils ($10^9/L$)	4.77 (4.0–5.85)	4.6 (3.9–5.6)	5.0 (4.2–6.2)	0.144
Lymphocytes ($10^9/L$)	2.1 (1.7–2.7)	2.04 (1.6–2.6)	2.1 (1.8–2.8)	0.263
Monocytes ($10^9/L$)	0.68 (0.54–0.78)	0.71 (0.5–0.88)	0.69 (0.6–0.84)	0.163
Hemoglobin (g/dL)	14.4 (12.6–15.2)	14.2 (12.5–15.1)	14.6 (12.9–15.5)	0.117
Platelet count ($10^9/L$)	248 (209–291)	249 (222–291)	239 (200–286)	0.239
Glucose (mg/dL)	108 (94–117)	106 (91–110)	116 (102–132)	0.234
Creatinine (mg/dL)	0.8 (0.8–1.04)	0.87 (0.8–1.0)	0.87 (0.8–1.1)	0.310
BUN (mg/dL)	16 (13–20)	15 (12–18)	16 (13–20)	0.480
eGFR (mL/min)	85 (70–94)	87 (77–96)	85 (66–94)	0.121
Albumin (g/dL)	4.1 (3.9–4.4)	4.2 (3.9–4.4)	4.1 (3.9–4.3)	0.198
AST (U/L)	18 (15–22)	18 (15–22)	17.5 (15–21)	0.716
ALT (U/L)	17 (13–24)	17 (12.2–24)	18 (13–25)	0.589
Na (mmol/L)	139 (137–141)	139 (137–140)	141 (138–142)	<0.001
CRP (mg/L)	0.8 (0.2–3.4)	0.5 (0.2–2.8)	1.03 (0.2–3.6)	0.791
Total cholesterol (mg/dL)	208 (185–241)	207 (179–241)	211 (185–241)	0.959
Triglycerides (mg/dL)	145 (113–200)	141 (123–204)	145 (109–208)	0.685
HDL cholesterol (mg/dL)	41 (34–49)	43 (34–52)	39 (33–44)	0.009
LDL cholesterol (mg/dL)	135 (104–154)	131 (103–153)	143 (107–155)	0.047
Osmolality (mOsm/kg)	289 (285–293)	288.1 (285–290)	293.2 (291–297)	<0.001

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; WBC: White blood cell count; BUN: Blood urea nitrogen; eGFR: Estimated glomerular filtration rate; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; Na: Serum sodium; CRP: C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

syndromes, our analysis focused exclusively on patients with stable, de novo coronary artery disease. This approach allowed us to better isolate the relationship between osmotic burden and chronic plaque morphology.

Most previous studies have examined serum osmolality in acute cardiovascular settings, and their findings provide important mechanistic and prognostic insights that are consistent with our

results in stable CAD. Tatlisu et al.^[8] found that hyperosmolality independently predicted longer hospitalization and poorer long-term survival in patients with ST-elevation myocardial infarction (STEMI). Yildiz et al.^[9] showed that elevated serum osmolality predicted contrast-induced nephropathy after primary percutaneous coronary intervention (PCI) in patients with STEMI.^[9] Farhan et al.^[10] reported that higher serum osmolality predicted

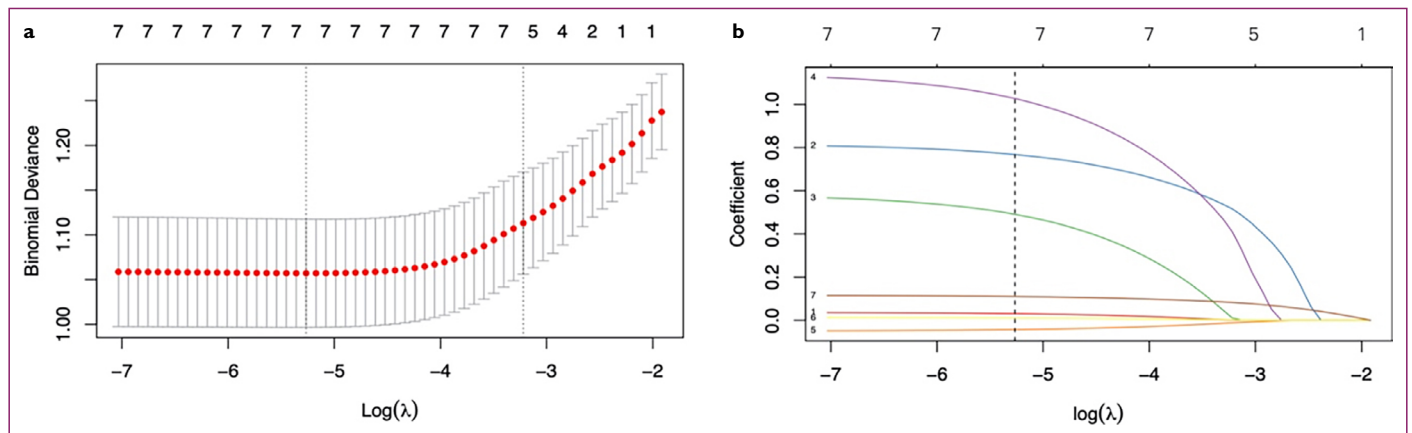


Figure 1. (a) Ten-fold cross-validation curve used to select the optimal value of the regularization parameter, lambda. The red dotted line represents lambda.min, corresponding to the lowest mean cross-validated error. (b) LASSO coefficient profile plot showing the shrinkage paths of the predictors. The vertical dotted line indicates the selected lambda.min, at which predictors with nonzero coefficients were included in the multivariable logistic regression model.

LASSO: Least absolute shrinkage and selection operator.

Table 3. Multivariable logistic regression analysis of predictors of a moderate-high SYNTAX score (>22)

Variables	OR	95% CI	p
Age (years)	1.038	1.003–1.076	0.037
Male sex	2.260	0.870–6.680	0.110
Smoking	1.790	0.960–3.410	0.070
COPD	3.140	1.040–10.110	0.047
HDL cholesterol (mg/dL)	0.950	0.920–0.980	0.002
LDL cholesterol (mg/dL)	1.013	1.004–1.022	0.004
Osmolality (mOsm/kg)	1.123	1.070–1.184	<0.001

Odds ratios (ORs), 95% confidence intervals (CIs), and p-values are shown for variables independently associated with a SYNTAX score>22, based on LASSO-selected predictors. SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; OR: Odds ratio; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

both acute kidney injury and 1-year mortality after PCI. Another study reported that higher plasma osmolality was independently associated with the occurrence of no-reflow in patients with STEMI undergoing primary PCI.^[11] Our study extends these observations from acute care settings by showing that calculated serum osmolality correlates with macrovascular lesion complexity in an entirely stable, ambulatory CAD population.

Hyperosmolar conditions may trigger vascular disturbances that promote atherosclerotic complexity. Elevated extracellular osmolality exerts multiple deleterious effects on cells by driving water efflux, which leads to cellular shrinkage and intracellular dehydration.^[12] This reduction in cell volume disrupts protein conformation and function, thereby impairing enzymatic activity. In addition, cellular shrinkage imposes substantial mechanical strain on both the cytoskeleton and the nucleus.^[12] At the same time, osmotic stress triggers the generation of reactive oxygen species, which accelerates smooth muscle cell proliferation and extracellular matrix remodeling within plaques.^[13] Moreover, hyperosmolar stimuli increase arginine vasopressin and its stable surrogate, copeptin, thereby promoting vasoconstriction, vascular stiffening, and adventitial fibrosis—features that contribute to tortuosity and calcification in advanced lesions.^[14] Collectively, these mechanisms may underlie the positive association observed between calculated serum osmolality and SYNTAX score in our cohort.

Although serum sodium remained within the normal range in both groups, patients with a SYNTAX score>22 exhibited higher sodium levels. This finding likely reflects multiple sodium-mediated effects on the coronary vasculature. Elevated sodium promotes arterial stiffness through extracellular matrix remodeling and vascular smooth muscle cell dysfunction—changes associated with more tortuous and calcified lesions.^[15] It also disrupts endothelial barrier integrity, increasing vascular permeability and facilitating lipid infiltration and local inflammation within plaques.^[16,17] Finally, sodium-induced increases in plasma osmolality trigger vasopressin release and sympathetic activation, raising vascular tone and shear stress—hemodynamic forces that drive complex coronary lesion formation.^[18]

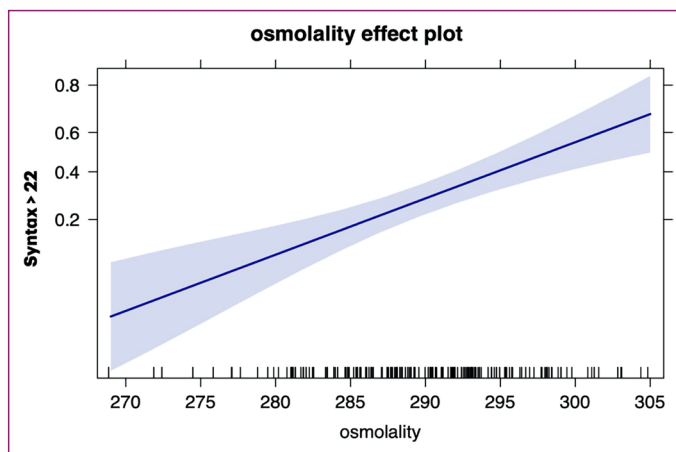


Figure 2. This graph demonstrates the adjusted effect of serum osmolality on the predicted probability of a SYNTAX score>22, derived from the final multivariable logistic regression model. The shaded area represents the 95% confidence interval.

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

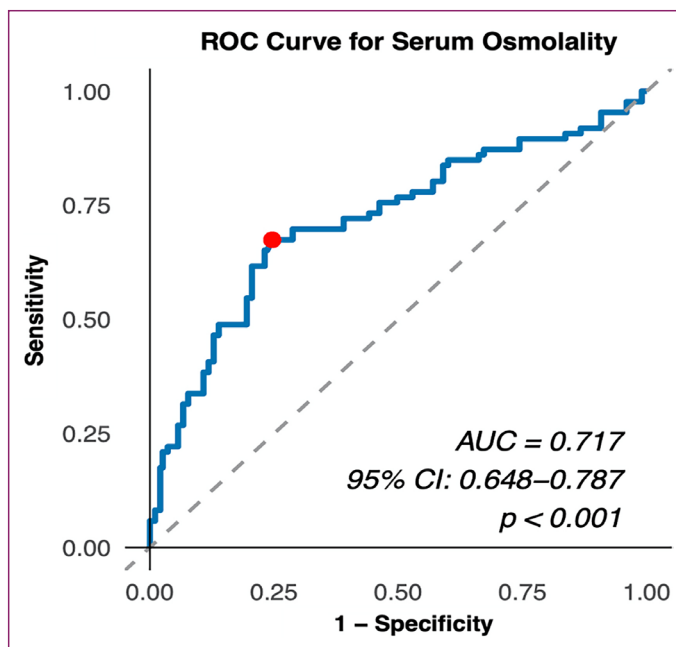


Figure 3. Receiver operating characteristic (ROC) curve showing the predictive ability of serum osmolality. The area under the curve (AUC) was 0.717 (95% CI, 0.648–0.787; $p < 0.001$), with an optimal cutoff of 291.6mOsm/kg (sensitivity, 0.67; specificity, 0.75).

CI: Confidence interval.

Similarly, despite excluding diabetic patients and maintaining glucose levels within the nondiabetic range, the SYNTAX score>22 cohort had higher fasting glucose levels. Even modest hyperglycemia promotes endothelial dysfunction by increasing mitochondrial reactive oxygen species production and activating protein kinase C pathways, which reduce nitric oxide bioavailability and impair vasodilatory capacity.^[19,20] High-normal glucose levels have also been shown to stimulate vascular smooth muscle cell proliferation and extracellular matrix remodeling through protein

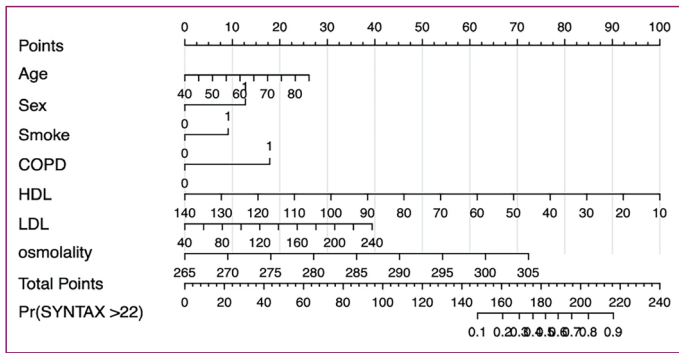


Figure 4. The nomogram was constructed based on the multivariable logistic regression model. Each predictor contributes a specific point value, and the total score is used to estimate the probability of a high SYNTAX score. Serum osmolality was one of the strongest contributors.

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; COPD: Chronic obstructive pulmonary disease; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

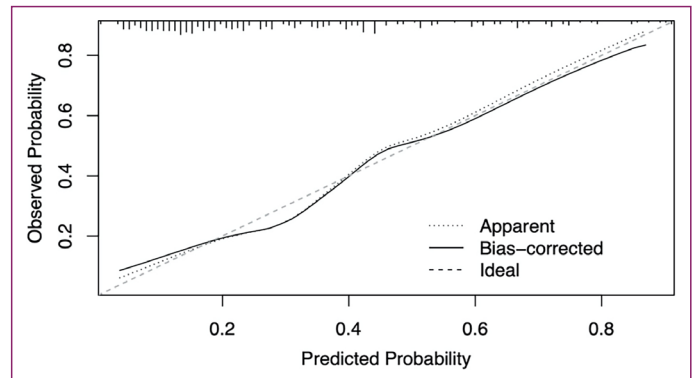


Figure 5. The calibration plot compares the predicted and observed probabilities of a high SYNTAX score. The bias-corrected curve (solid line) closely follows the ideal 45-degree line (dashed), indicating good model calibration. Results are based on 1000 bootstrap samples.

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

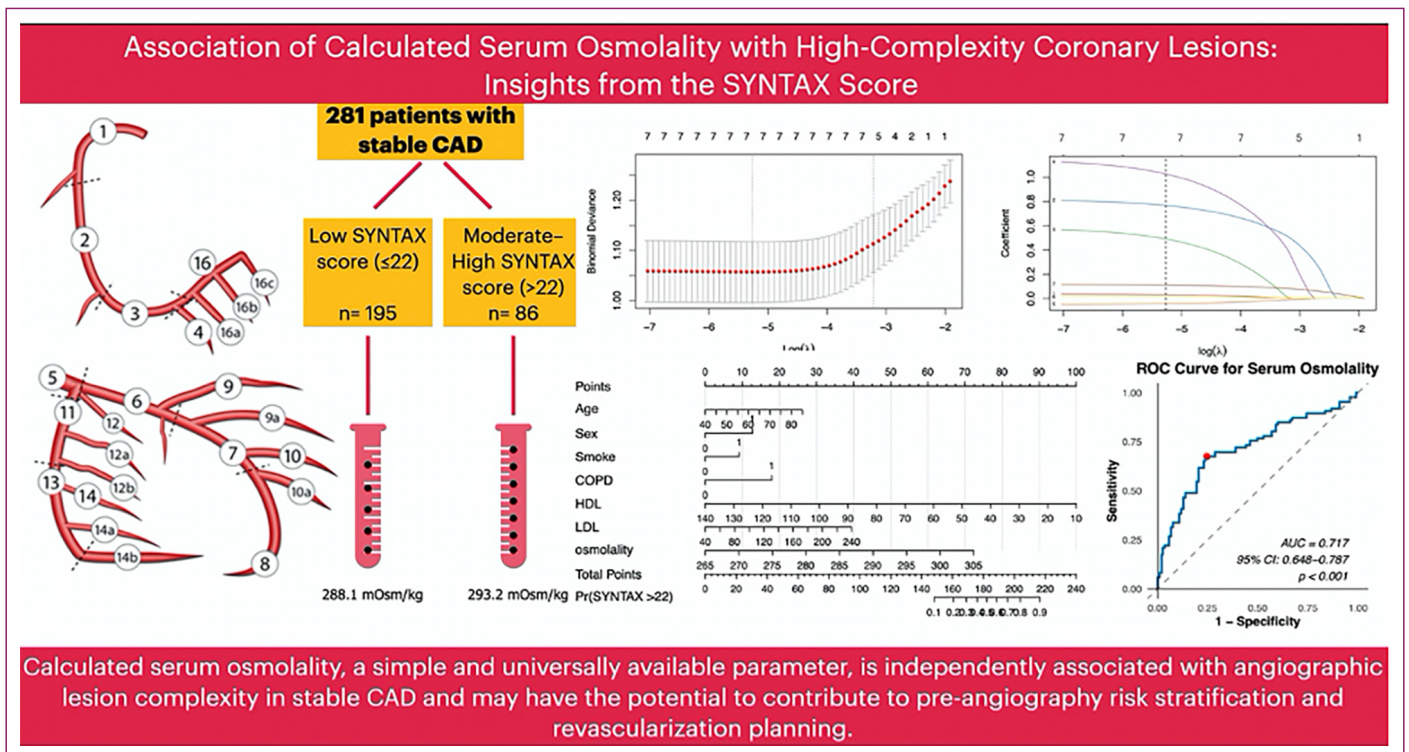


Figure 6. Graphical abstract.

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

kinase C–mediated pathways, contributing to arterial stiffening and calcification characteristic of complex coronary lesions.^[21] In contrast, although elevated blood urea nitrogen (BUN) levels have been independently linked to adverse cardiovascular outcomes in previous studies, we found no significant difference between groups.^[22] This may be attributable to the exclusion of patients with chronic kidney disease from our cohort.

Calculated osmolality, which can be derived from routine laboratory measurements without additional cost or patient burden, may serve as a pragmatic biomarker for risk stratification in stable

CAD. The nomogram we developed integrates osmolality with other key predictors to generate individualized estimates of lesion complexity, which could inform the need for advanced imaging modalities or guide revascularization strategy decisions. Because high SYNTAX scores are associated with greater procedural risk and worse long-term outcomes, early identification of these patients using a simple laboratory measure is clinically appealing.

Our model also reaffirmed the importance of established predictors: advanced age, low HDL, and high LDL cholesterol were significantly associated with lesion complexity, consistent with

large registries linking dyslipidemia to multivessel and complex disease patterns.^[23–26] COPD emerged as an independent risk marker, likely reflecting chronic systemic inflammation and oxidative injury inherent to airway disease—mechanisms known to exacerbate atherosclerosis and plaque instability.^[27] Our study population comprised patients with stable CAD without diabetes, advanced renal disease, or use of medications known to substantially influence serum osmolality. This design aimed to minimize confounding effects on osmolality. The observed independent association between calculated serum osmolality and SYNTAX score in this cohort suggests that this routinely available parameter may be linked to the underlying pathophysiology of coronary lesion complexity. Further studies in broader populations are needed to validate these findings and to assess the role of directly measured osmolality.

Limitations

This single-center retrospective study limits generalizability. Although the formula used is standard and has shown good correlation with direct measurement in many settings, the osmolal gap may still be clinically significant. Medication effects on fluid balance were not uniformly recorded and may have influenced the results. The exclusion of patients with diabetes mellitus may have introduced selection bias and may limit the external validity and generalizability of the findings to broader clinical populations. Prospective multicenter studies with larger and more diverse cohorts are needed to validate these observations and to explore whether targeting osmotic balance can modify the progression of complex coronary disease.

Conclusion

Calculated serum osmolality is independently associated with coronary lesion complexity, as defined by a high SYNTAX score, in patients with stable CAD. Its ready availability from routine laboratory testing makes it a practical biomarker for enhancing risk stratification and guiding individualized revascularization strategies.

Disclosures

Ethics Committee Approval: The study was approved by the Izmir Katip Çelebi University Health Research Ethics Committee (no: 0473, date: 17/07/2025).

Informed Consent: Written informed consent was waived by the review board.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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