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Integrating the STOP-BANG Score and Clinical Data to Predict Cardiovascular Events After Infarction

A Machine Learning Study

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BACKGROUND: OSA conveys worse clinical outcomes in patients with coronary artery disease. The STOP-BANG score is a simple tool that evaluates the risk of OSA and can be added to the large number of clinical variables and scores that are obtained during the management of patients with myocardial infarction (MI). Currently, machine learning (ML) is able to select and integrate numerous variables to optimize prediction tasks.

RESEARCH QUESTION: Can the integration of STOP-BANG score with clinical data and scores through ML better identify patients who experienced an in-hospital cardiovascular event after acute MI?

STUDY DESIGN AND METHODS: This is a prospective observational cohort study of 124 patients with acute MI of whom the STOP-BANG score classified 34 as low (27.4%), 30 as intermediate (24.2%), and 60 as high (48.4%) OSA-risk patients who were followed during hospitalization. ML implemented feature selection and integration across 47 variables (including STOP-BANG score, Killip class, GRACE score, and left ventricular ejection fraction) to identify those patients who experienced an in-hospital cardiovascular event (ie, death, ventricular arrhythmias, atrial fibrillation, recurrent angina, reinfarction, stroke, worsening heart failure, or cardiogenic shock) after definitive MI treatment. Receiver operating characteristic curves were used to compare ML performance against STOP-BANG score, Killip class, GRACE score, and left ventricular ejection fraction, independently.

RESULTS: There were an increasing proportion of cardiovascular events across the low, intermediate, and high OSA risk groups ($P = .005$). ML selected 7 accessible variables (ie, Killip class, leukocytes, GRACE score, c reactive protein, oxygen saturation, STOP-BANG score, and N-terminal prohormone of B-type natriuretic peptide); their integration outperformed all comparators (area under the curve, 0.83 [95% CI, 0.74-0.90]; $P < .01$).

INTERPRETATION: The integration of the STOP-BANG score into clinical evaluation (considering Killip class, GRACE score, and simple laboratory values) of subjects who were admitted for an acute MI because of ML can significantly optimize the identification of patients who will experience an in-hospital cardiovascular event.

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KEY WORDS: acute myocardial infarction; cardiovascular events; feature selection; machine learning; OSA; STOP-BANG score

ABBREVIATIONS: AF = atrial fibrillation; AUC = area under the curve; CRP = c reactive protein; IGR = information gain ranking; GRACE = Global Registry of Acute Coronary Events; LVEF = left ventricular ejection fraction; MI = myocardial infarction; ML = machine learning; PCI = percutaneous coronary intervention

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Take-home Points

Study Question: Can the integration of STOP-BANG score with clinical data and scores through machine learning better identify patients who will experience an in-hospital cardiovascular event after acute myocardial infarction?

Results: Machine learning modelling including clinical (laboratory) variables, Killip class, GRACE, and STOP-BANG scores significantly outperforms the individual scores and left ventricular ejection fraction.

Interpretation: The integration of the STOP-BANG score into clinical evaluation (considering Killip class, GRACE score, and simple laboratory values) of patients who are admitted for an acute MI through machine learning can significantly optimize the identification of patients who will experience an in-hospital cardiovascular event.

OSA represents a severely underdiagnosed (approximately 80%) form of sleep-disordered breathing,[1-6] which importantly associates to several forms of cardiovascular disease.[7] Notably, approximately 44% to 69% of patients presenting to the ED with an acute myocardial infarctionMI fulfill polysomnographic criteria for at least mild OSA.[8-10] This becomes relevant when considering that patients with coronary artery disease and untreated OSA show a higher proportion of adverse cardiovascular outcomes.[10-13] However, very few patients undergo polysomnographic evaluation during hospitalization for an acute coronary syndrome, and an alternative can be found in the assessment of the easy-to-apply STOP-BANG questionnaire, which constitutes a validated method for OSA-risk stratification.[14] The STOP-BANG score evaluates Snoring, Tiredness, Observed-apnea, blood Pressure, Body-mass-index, Age, Neck circumference, and Gender and assigns a low-, intermediate-, or high-risk of OSA.

In parallel, it has been recognized that a very large number of variables that include demographics, anthropometrics, laboratory values, and hemodynamic measurements are collected regularly in the management of patients with acute MI. In fact, some of these have been integrated (to varying degrees and through linear modeling) into clinical scores, such as the Killip class and the GRACE (Global Registry of Acute Coronary Events) score, to gauge mortality risk after an acute coronary syndrome.[15,16]

Recently, the implementation of machine learning (ML) algorithms has begun to revolutionize data analysis in cardiovascular and respiratory medicine.[17-19] ML offers the possibility to explore, select, and integrate large amounts of interrelated variables, while extracting nonlinear dependencies (patterns) that are useful to optimize classification and prediction tasks[20] beyond the capacity of traditional statistics.

Given the suspected additive value of the STOP-BANG tool (as a proxy for the risk of OSA) to the numerous available clinical variables and scores (Killip and GRACE score) in the risk-stratification of patients who are hospitalized for an acute MI, exploring the implementation and performance of ML for such integration is warranted.

Hence, the present study aimed to implement and evaluate the performance of ML in the integration of the STOP-BANG score with available clinical variables and derived-scores for the identification of patients who experienced cardiovascular events during their hospitalization for acute MI. Complementarily, we compared ML performance with that of traditional linear modeling considering the involved scores (Killip and GRACE score) and left ventricular ejection fraction (LVEF), independently.

Methods

We prospectively studied 124 patients who were admitted to the coronary unit with acute MI.[21] The study was approved by the institutional research and ethics committee (protocol ID: 17-1024) in accordance with the guidelines provided by the Declaration of Helsinki' all subjects provided informed consent.

Eligible patients were at least 18 years of age with a symptom onset-to-hospital admission time of <48 hours. Patients with active OSA treatment were excluded. Patients received standard care with dual

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antiplatelet therapy, anticoagulation, high-dose statin, angiotensin-converting enzyme inhibitors, and beta-blockers (unless contraindicated).

Clinical Variables

Demographic (age, sex) and anthropometric variables, cardiovascular history (prior MI, percutaneous coronary intervention [PCI], stroke, atrial fibrillation [AF], and hospitalization for congestive heart failure), risk factors (diabetes mellitus, hypertension, dyslipidemia, and smoking), hemodynamics (blood pressure, heart rate, and oxygen saturation), angiographic and PCI-related features (culprit-vessel, multivessel disease, thrombolysis in myocardial infarction-flow, thrombolysis in myocardial infarction myocardial perfusion grade, and no-reflow phenomenon[22]), LVEF, and laboratory values (erythrocyte-count and distribution, leucocyte-count, hemoglobin level, hematocrit level, platelets, sodium, potassium, chloride, creatinine, glucose, albumin, c reactive protein (CRP), cholesterol, triglycerides, glucose, HbA1C, NT-proBNP at admission, and peak troponin I) were retrieved.

STOP-BANG Score

The modified STOP-BANG questionnaire (available here) was used to evaluate the risk of OSA.[14,23] The score was operationalized into three groups: low (0 to 2), intermediate (3 to 4), or high (5 to 8) OSA risk. Patients who answered positively at least 2 of the 4 STOP questions and who had at least one of the following: male sex, BMI$>$ 35 kg/m^2, or neck circumference $\geq$43 cm ($\geq$41 cm in women) were also classified as high-risk individuals.[23]

Killip class and GRACE Score

MI-related clinical variables were integrated into the Killip class[24] and the GRACE score (age, heart rate, systolic BP, creatinine, cardiac arrest at admission, ST-segment deviation, abnormal cardiac enzymes, and Killip class), accordingly.

In-hospital Cardiovascular Events: Outcomes

After admission and definitive treatment, patients were followed throughout their hospitalization for the occurrence of a composite outcome meaning at least one of the following cardiovascular events: all-cause death, ventricular arrhythmias (ie, ventricular fibrillation or sustained ventricular tachycardia that required IV drugs or cardioversion/defibrillation), new-onset AF, recurrent or refractory angina (ie, chest pain occurring $>$48 hours after PCI or that required dose titration of IV nitrates), reinfarction, stroke, worsening heart failure (defined as either new onset pulmonary edema or worsening signs and/or symptoms of heart failure that require treatment intensification or mechanical ventilation support) or cardiogenic shock (clinical criteria: hypotension [systolic pressure $<$90 mm Hg for at least 30 minutes or need for supportive measures to maintain it equal of $>$90 mm Hg], end-organ hypoperfusion [cool extremities or a urine output of $<$30 mL/hr, and a heart rate of $\geq$60 beats/min], cardiac index $\leq$2.2 L/m/m^2 [Fick Method], and evidence of pulmonary congestion on chest radiography).[25]

Machine Learning

Data Preprocessing and Cross-Validation: ML analytics were performed in the Waikato Environment for Knowledge Analysis (WEKA open-source software, version 3.8.3, Hamilton, New Zealand). A 5-fold cross-validation policy was applied to feature selection and model development (training-testing splits). All continuous variables were normalized to convey their distribution in an 0-to-1 range and input through the ML-workflow. Default imputation was performed by the WEKA platform in cases with missing values (population mean for continuous variables or an alternative "missing" label for categoric ones).

Feature Selection: Forty-seven features (variables) including the STOP-BANG score, Killip class, and GRACE score were input for variable exploration and selection. The information gain-based method known as information gain (entropy) ranking (IGR) was implemented for feature selection (criteria $>$0.05[20,26]) to consider the variable as contributing to posterior modeling. IGR evaluates the loss-of-entropy (unpredictability) gained by splitting the data through each evaluated feature. The features that, in compound, will potentially better split data will rank higher and provide a useful input to modelling.

Modeling (Prediction): The selected features were integrated through an ensemble boosting algorithm (LogitBoost) with the use of decision stumps. This ML approach has demonstrated adequate and consistent performance in the integration of multiple variables in prediction tasks.[20,26,27] In brief, the algorithm iteratively combines weak base classifiers by adjusting their relevance in identifying cases from noncases according to misclassifications (errors in relation to the known outcome label) during the training process (ie, wrongly classified data points will have more relevance in the evaluation of the next weak classifier; correct classifications will not). The result of this process is a strong compound classifier that outputs a pseudo-probability score ultimately binarized for the outcome variable (occurrence of the composite endpoint of in-hospital cardiovascular events in this case). The final result provides a trained model that can be provided with data (the selected features) from a new patient and outputs a prediction of the group to which it belongs.

Statistical Analysis

All continuous variables were described as means $\pm$ corresponding SD. Categoric variables were expressed as frequencies and percentages. Descriptively, unpaired *t*-tests were used to evaluate differences in baseline characteristics between patients who did and did not present the outcome of interest, and supplementary, one-way analyses with follow up-adjusted pairwise comparisons or their corresponding nonparametric counterparts were used to evaluate differences in continuous variables across STOP-BANG OSA-risk categories. Pearson χ^2 test or the Fisher exact test were used to evaluate differences in proportions for categoric variables.

ML performance was evaluated through precision, recall, accuracy, and the F1-score (metrics that pertain to ML evaluation). Receiver operating characteristic curve analyses evaluated ML discrimination performance through area under the curve (AUC) that was compared against those from logistic regression analyses of the STOP-BANG score, Killip class, GRACE score, and LVEF (as robust proxies of acute cardiovascular risk) independently. These comparisons were performed in a pairwise manner according to the method by DeLong et al.[28] A probability value of $<$ .05 was considered statistically significant. These statistical analyses were performed with MedCalc Statistical Software (version 18.2.1; MedCalc Software bvba, Ostend, Belgium).

Results

In total, 124 eligible patients (22 women and 102 men) were included (mean age, 62 $\pm$ 11.6 years). Table 1 shows the demographic, clinical, laboratory, hemodynamic, and angiographic variables in patients who did (n = 46) and did not present (n = 78) the

composite outcome. There was a balanced distribution of clinical variables overall, and no significant differences were found in demographics, cardiovascular risk factors, myocardial infarction characteristics, or treatment. Conversely, we found significant differences between patients with and without the outcome of interest in the STOP-BANG ($P = .001$) and GRACE ($P < .001$) scores, in LVEF ($P < .001$), NT-proBNP ($= = .019$), creatinine ($P = .004$), and the occurrence of no-reflow phenomenon ($P = .007$).

According to the STOP-BANG score, there were 34 patients(27.4%) at low risk, 30 patients (24.2%) at intermediate risk, and 60 patients (48.4%) at high risk of OSA. The profile of all variables across these groups is shown in Table 2. There were no differences between OSA-risk groups regarding the presence of risk factors, although there were significantly fewer women (38.2% vs 16.7% vs 6.7%; $P < .001$) and more patients with hypertension (23.5% vs 63.3% vs 80%; $P < .001$) at the high-risk end. Patients who were at high risk for OSA had lower oxygen saturations at admission

TABLE 1] Clinical Variables in Patients With and Without at Least One In-hospital Cardiovascular Event, Truncated for Space

Variable	Patients With an In-hospital Event (n = 46)	Patients Without In-hospital Events (n = 78)	*P* Value
Women, No. (%)	7 (15.2)	15 (19.2)	.63
Age, mean (± SD), y	61.2 (10.29)	62.3 (12.32)	.60
Hypertension, No. (%)	32 (69.6)	43 (55.1)	.13
Diabetes mellitus, No. (%)	27 (58.7)	34 (43.6)	.14
Previous myocardial infarction, No. (%)	8 (17.4)	22 (28.2)	.19
Previous percutaneous coronary intervention, No. (%)	4 (8.7)	14 (17.9)	.19
Prior hospitalization for heart failure, No. (%)	2 (4.3)	1 (1.3)	.56
ST-segment elevation MI reperfusion type, No. (%)			.59
Primary percutaneous coronary intervention	8 (21)	17 (34)	
Successful thrombolysis	5 (13)	6 (12)	
Failed thrombolysis	6 (16)	8 (16)	
Nonreperfused	19 (50)	19 (38)	
ST-segment elevation MI localization, No. (%)			.39
Anterior	19 (50)	18 (36)	
Inferior	15 (39)	27 (54)	
Other	4 (11)	5 (10)	
Multivessel disease, No. (%)	29 (63.0)	40 (51.3)	.43
No-reflow phenomenon, No. (%)	12 (26.1)	5 (6.4)	.007[a]
Peak troponin I, mean (± SD), ng/mL	73.03 (58.14)	51.75 (55.71)	.05
Basal NT-ProBNP, mean (± SD), pg/mL	2,874 (4,778)	795 (2,785)	.001[a]
Hemoglobin, mean (± SD), g/dL	14.6 (2.09)	15.1 (2.07)	.224
Leukocytes ×1000/μL	13.2 (5.4)	10.5 (2.9)	.002[a]
Serum creatinine, mean (± SD), mg/dL	1.35 (0.48)	1.12 (0.38)	.004[a]
Left ventricular ejection fraction, mean (± SD), %	35.1 (12.65)	46.2 (10.66)	< .001[a]
Killip class, mean (± SD)	2.15 (1.1)	1.25 (0.5)	< .001[a]
GRACE score, mean (± SD)	163.2 (40.28)	132.3 (33.01)	< .001[a]
STOP-BANG score, mean (± SD)	4.6 (1.77)	3.5 (1.61)	.001[a]

GRACE = Global Registry of Acute Coronary Events; NT-ProBNP = N-terminal prohormone of B-type natriuretic peptide.
[a]Indicates statistical significance.

TABLE 2] Variables Across OSA-Risk Groups

Variable	OSA Risk			*P* Value
	Low (n = 34)	Intermediate (n = 30)	High (n = 60)	Pairwise Comparisons
Demographic characteristics, cardiovascular history, and risk factors				
Age, mean (± SD), y	64.6 (12.84)	63.4 (10.06)	59.6 (11.25)	.99[a] .14[b] .41[c]
Women, No. (%)	13 (38.2)	5 (16.7)	4 (6.7)	< .001
BMI, mean (± SD), kg/m^2	24.9 (3.11)	27.6 (3.25)	30.4 (5.47)	.07 [a] < .001[b] .015[c]
Neck circumference, mean (± SD), cm	38.4 (2.53)	42.1 (3.11)	45.1 (3.64)	< .001[a] < .001[b] < .001[c]
Diabetes mellitus, No. (%)	16 (47.1)	14 (46.7)	31 (51.7)	.92
Hypertension, No. (%)	8 (23.5)	19 (63.3)	48 (80.0)	< .001
Dyslipidemia, No. (%)	15 (44.1)	15 (50.0)	30 (50.0)	.89
Smoking history, No. (%)	16 (47.1)	17 (56.7)	35 (58.3)	.58
Previous MI, No. (%)	12 (35.3)	7 (23.3)	11 (18.3)	.19
Previous PCI, No. (%)	7 (20.6)	6 (20.0)	5 (8.3)	.17
Heart failure hospitalization, No. (%)	1 (2.9)	0 (0)	2 (3.3)	.80
Stroke, No. (%)	0 (0)	0 (0)	2 (3.3)	.36
Atrial fibrillation, No. (%)	0 (0)	1 (3.3)	1 (1.7)	.73
STOP-BANG score, mean (± SD)	1.8 (0.39)	3.4 (0.67)	5.3 (1.20)	< .001
Clinical variables and laboratory values				
Systolic BP, mean (± SD), mm Hg	126.6 (20.04)	133.2 (23.63)	132.4 (24.71)	.43
Diastolic BP, mean (± SD), mm Hg	79.1 (11.79)	79.1 (15.65)	80.5 (16.69)	.88
Heart rate, mean (± SD), beats/min	76.4 (19.29)	77.2 (22.77)	76.3 (20.54)	.98
O_2 saturation,[a] mean (± SD), %	93.2 (3.99)	91.3 (4.17)	89.8 (5.99)	.01
Peak troponin I, mean (± SD), ng/mL	51.20 (51.276)	56.59 (62.843)	65.95 (57.898)	.47
Basal NT-Pro BNP, mean (± SD), pg/mL	2,356 (6056)	1,066 (3700)	1,375 (3596)	.219
Hemoglobin, g/dL	14.3 (2.4)	14.7 (2.1)	15.3 (1.8)	.08
Hematocrit, mean (± SD), %	41.5 (6.43)	40.54 (9.13)	43.9 (4.96)	.04
Leucocytes, mean (± SD), 10^3/L	10.69 (3.47)	10.73 (3.23)	12.58 (4.78)	.04
Platelets, mean (± SD), 10^3/L	234.82 (55.43)	241.43 (55.27)	237.55 (74.75)	.92
Creatinine, mean (± SD), mg/dL	1.09 (0.426)	1.21 (0.429)	1.27 (0.425)	.15
Glucose, mean (± SD), gr/dL	159.8 (82.72)	180.2 (84.09)	199.4 (112.55)	.18
C-reactive protein, mean (± SD), mg/L	60.3 (87.3)	67.1 (104.83)	74.21 (102.91)	.82
% HBA1C mean (± SD)	6.8 (1.65)	6.9 (1.88)	7.3 (2.09)	.62
MI variables, management, and prognostic scores				
Nocturnal-onset of symptoms, No. (%)	7 (20.6)	7 (23.3)	23(38.3)	.032
STEMI/NSTEMI, No.	23/11	20/10	45/15	.63
STEMI reperfusion, No (% within STEMI)				.62
Primary PCI	6 (26.1)	4 (20.0)	15 (33.3)	
Successful thrombolysis	5 (21.7)	2 (10.0)	4 (8.9)	
Failed thrombolysis	2 (8.7)	4 (13.3)	8 (17.8)	

(Continued)

TABLE 2] *(Continued)*

Variable	OSA Risk			*P* Value
	Low (n = 34)	Intermediate (n = 30)	High (n = 60)	Pairwise Comparisons
Nonreperfused	10 (43.5)	10 (50.0)	18 (40.0)	
Killip class, No. (%)				.030
I	23 (67.6)	21 (70.0)	33 (55.0)	
II	6 (17.6)	9 (30.0)	16 (26.7)	
III	4 (11.8)	0 (0)	3 (5.0)	
IV	1 (2.9)	0 (0)	8 (13.3)	
GRACE score, mean (± SD)	148 (35)	139 (35)	144 (43)	.98
Left ventricular ejection fraction, % (± SD)	38.9 (12.93)	45.9 (11.70)	40 (12.90)	.19[a]
				.99[b]
				.22[c]
Coronary angiography and PCI-related variables (when available)	n = 29	n =27	n = 58	
Multivessel disease, No. (%)	22 (76)	16 (59)	31 (53)	.035
Culprit artery, No. (%)				.31
LAD, No. (%)	10 (34.5)	12 (44.4)	24 (41.4)	
LCx, No. (%)	5 (17.2)	4 (14.8)	7 (12.1)	
RCA, No. (%)	14 (48.3)	11 (40.7)	26 (44.8)	
Culprit artery TIMI flow, No. (%)				.13
0	14 (48.3)	7 (24.1)	30 (51.7)	
1	3 (10.3)	2 (7.4)	4 (6.9)	
2	1 (3.4)	7 (24.1)	9 (15.5)	
3	11 (37.9)	11 (40.7)	14 (24.1)	
Final TIMI flow, No. (%)				.92
0	1 (3.4)	2 (7.4)	4 (6.9)	
1	1 (3.4)	0 (0)	1 (1.7)	
2	3 (10.3)	3 (11.1)	8 (13.8)	
3	20 (68.9)	20 (74.1)	41 (70.7)	
Final TMP grade, No. (%)				.31
0	2 (6.9)	2 (7.4)	7 (12.1)	
1	0 (0)	3 (11.1)	9 (15.5)	
2	6 (20.7)	3 (11.1)	6 (10.3)	
3	16 (55.2)	17 (58.6)	32 (55.2)	
No-reflow phenomenon, No. (%)	3 (10.3)	3 (11.1)	11 (18.9)	.51
Admission to PCI time, No. (%)				.17
<12 h	9 (31.0)	9 (33.3)	30 (51.7)	
12 to 24 h	6 (20.7)	5 (18.5)	4 (6.9)	
>24 h	14 (48.3)	13 (48.1)	24 (41.4)	
STEMI door to balloon time, min (± SD)	82.2 (16.51)	99.3 (42.09)	95.4 (39.53)	.98

HBA1C = hemoglobin A1C; LAD = left anterior descending artery; LCx = left circumflex artery; NSTEMI = non-ST-segment elevation MI; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment elevation MI; TIMI = thrombolysis in myocardial infarction; TMP = TIMI myocardial perfusion. See Table 1 legend for expansion of other abbreviations.

[a]Low vs intermediate.

[b]Low vs high.

[c]Intermediate vs high.

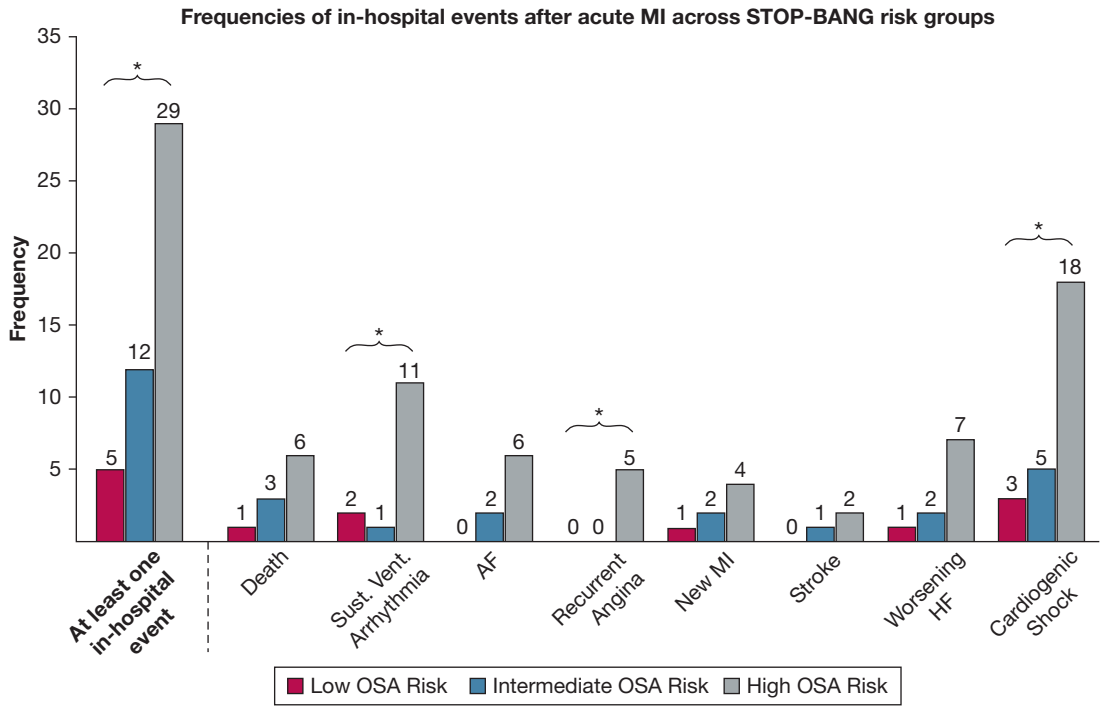

Figure 1 – *In-hospital cardiovascular events across OSA-risk groups. The asterisk indicates probability value of < .05. AF = atrial fibrillation; HF = heart failure; MI = myocardial infarction; Sust. Vent. = sustained ventricular.*

(89.8% ± 5.99% vs 93.2% ± 3.99%; $P = .008$) and a higher Killip class ($P = .030$) than patients at low risk for OSA. There were no significant differences in hemodynamics and infarction type (ST-segment elevation MI or non-ST-segment elevation MI) between STOP-BANG groups.

Figure 1 shows the frequency and type of outcomes in each OSA-risk group. The proportion of occurrence of the composite outcome (at least 1 in-hospital cardiovascular event) was significantly lower in patients with low OSA-risk (STOP-BANG score ≤2) (14.7%) when compared with the intermediate- (45.6%) and high-risk groups (48.3%) ($P = .005$). The proportions of occurrence of sustained ventricular arrhythmias ($P = .028$) and recurrent/refractory angina ($P = .024$) significantly increased with OSA risk. Remarkably, cardiogenic shock showed the highest incidence and largest difference between groups ($P = .008$). Death, new-onset AF, reinfarction, stroke, and worsening heart failure showed no significant differences across OSA-risk groups.

The cross-validated ML feature selection process demonstrated that the most relevant attributes (variables) for subsequent ML modelling were Killip class, leucocyte count, the GRACE score, CRP, oxygen saturation, the STOP-BANG score, and NT-proBNP levels. At the same time, the least relevant features were chloride, erythrocyte count, potassium, platelet count (mainly laboratory measurements), and age. Figure 2 shows the feature selection rank-based process.

The ML algorithm considering the seven selected features documented a precision of 72%, recall of 85%, accuracy of 77%, and F1-score of 0.67. The corresponding ML-AUC was 0.83 (95% CI, 0.74-0.90], which significantly outperformed all other comparators, namely: Killip class (AUC, 0.73 [(95% CI, 0.63-0.83]), GRACE (AUC, 0.70 (95% CI, [0.60-0.80]), STOP-BANG score (AUC, 0.69 [(95% CI, 0.59-0.78]) and LVEF (AUC, 0.66 [(95% CI, 0.54-0.78]) (all pairwise $P < .01$). The independent contribution of the STOP-BANG score to ML modelling was explored by training an independent model using the same features without STOP-BANG, which significantly decreased its discriminative performance (AUC, 0.79 [(95% CI, 0.70-0.88]). Figure 3 shows the comparative receiver operating characteristic-curve analyses. Independently, the STOP-BANG and GRACE scores showed comparable performance ($P > .05$).

Discussion

In the present study, we implemented an ML algorithm to explore select and integrate a large number of clinical

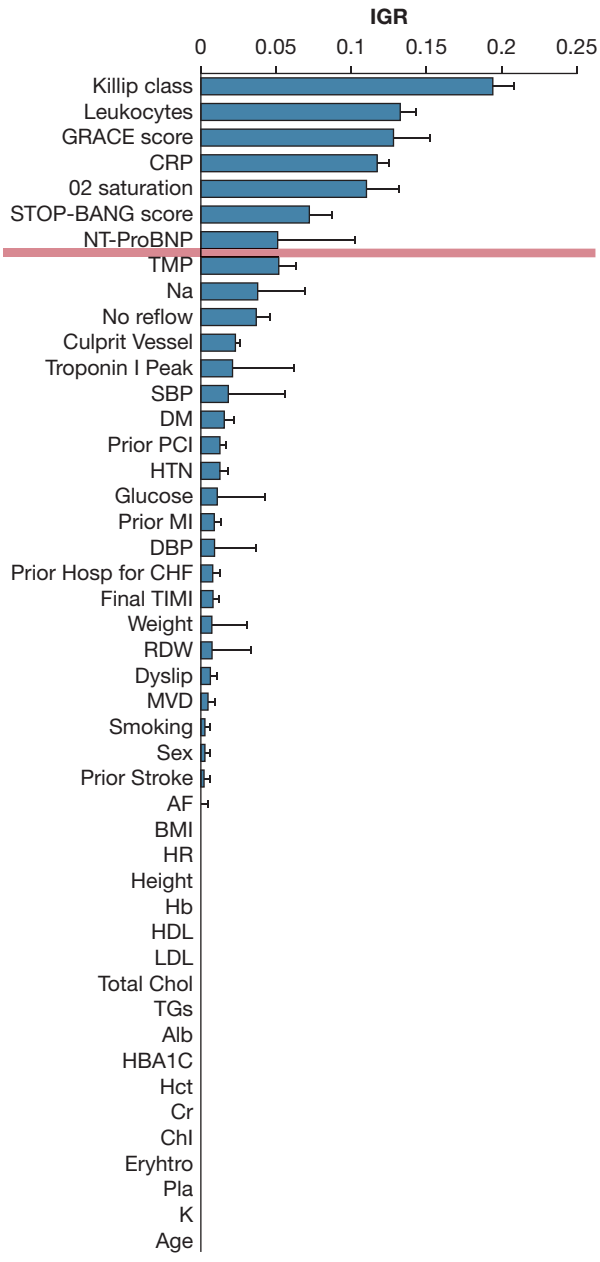

Figure 2 – *Machine learning feature selection based on 5-fold cross-validated information gain ranking.*

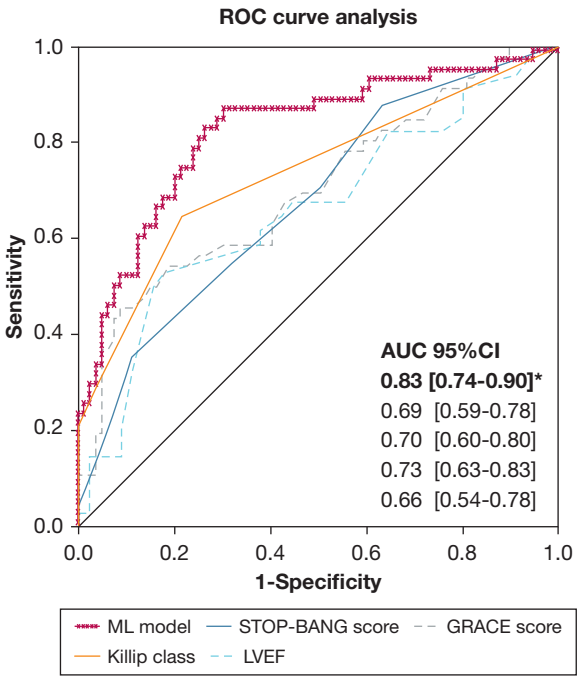

Figure 3 – *Receiver operating characteristic analysis and comparative performance of the integrated machine learning model, the STOP-BANG score, the GRACE score, the Killip class, and left ventricular ejection fraction in discriminating between patients who presented an in-hospital cardiovascular event after the acute myocardial infarction. AUC = area under the curve; LVEF = left ventrical ejection fraction; ROC = receiver operating characteristic. See Figure 1 legend for expansion of other abbreviation.*

variables and scores (STOP-BANG, Killip, and GRACE) available in patients who were hospitalized because of an acute MI to identify those who experienced a cardiovascular event during their hospitalization. Our approach incorporates two novel concepts in this area. One, the STOP-BANG score demonstrated an added value in the identification of patients who were admitted with an acute MI who were at risk of potentially fatal in-hospital events, and two, the application of ML analytics was used to optimize discriminative performance for such clinical purpose.

We studied patients who were admitted with an acute MI to the coronary unit of our institution and observed that 73% of them showed at least an intermediate risk of OSA by the STOP-BANG score. This prevalence is in line with the results reported by McCormack et al[29] on the prevalence of significant STOP-BANG scores among patients with MI (approximately 75%) and by the largest prospective study to date, the Sleep and Stent study, in which among 1311 patients who were treated with PCI, 45.3% showed OSA (ie, apnea-hypopnea index ≥15[10]). Notably, this estimates link with a clinical profile reflected in the worrisome epidemiologic estimates of overweight and obesity in Mexico[30] and worldwide. Moreover, the fact that our prevalence results approached those of previous studies, despite having used only a screening tool (STOP-BANG), supports the value of the STOP-BANG score in this population. Therefore, we speculate that roughly one-half of the patients who were admitted for an acute MI have approximately an 80% probability of being diagnosed with OSA if a sleep study would have been done. We believe this assumption should encourage follow-up evaluation for the integral treatment of these patients.

Our ML-workflow delivered a seven-variable structure from feature selection, which is a modern approach to gauge variable importance accounting for high-dimensional interactions otherwise ignored in conventional linear modeling (which bases variable inclusion in probability values). The evaluation of the IGR was incorporated with clinical reasoning to establish a panel of features that can be obtained easily during initial workup of patients with MI (ie, physical measurements and a basic laboratory panel). Notably, our selected variable subset included the STOP-BANG score, Killip class, and GRACE score, which underlines the independent relevance of these approaches in flagging individuals who are at risk of adverse short-term outcomes (eg, death). Furthermore, acute phase markers (leukocytes, CRP, oxygen saturation, and NT-proBNP) also significantly contributed to ML modeling, which supports the utility of such measurements in this setting. Of note, the results are clear that variables that are included in the aforementioned scores would also be individually relevant if such scores were not included for ML modelling. In this case, we opted for analyzing scores because it is common clinical practice to document them and therefore can be easily input as single variables.

ML substantially outperformed the individual clinical scores (Killip class, GRACE, and STOP-BANG score itself) and LVEF (one of the most robust predictors of outcome) in the identification of patients who experienced an in-hospital cardiovascular event after standard-of-care MI treatment, at the individual level. This is a remarkable gain in discriminative capacity when considering the isolated performance of currently used clinical scores.

Given the ML model structure, our results suggest that the STOP-BANG score can be a relevant and worthwhile addition to the acute setting evaluation. The STOP-BANG questionnaire was created to aid in OSA-risk stratification; because OSA itself is highly suspected to worsen prognosis in patients with cardiovascular disease, it follows that the application of the questionnaire can expand the clinical characterization of patients with an acute MI because they may be at increased risk of potentially fatal short-term outcomes. Our results demonstrate the relevance of the STOP-BANG score through the significant differences found in the rate of adverse outcomes across OSA-risk categories.

There is an ongoing controversy around the direction of the influence of OSA on the occurrence of cardiovascular events, which includes MI.[31] Recently, a Spanish study proposed that OSA may exert a protective effect in the context of MI (based on peak troponin-I levels[32]), maybe through ischemic preconditioning.[33] Our study concentrated on the risk of OSA that was evaluated through the STOP-BANG questionnaire rather than on patients already diagnosed with the disease. Therefore, results should be understood contextually; we found no significant difference in the peak troponin-I levels between patients with and without an in-hospital event. At the same time, we noticed anthropometric differences with their population (STOP-BANG components [BMI and neck circumference]). Therefore, we speculate that the operating pathologic mechanisms in patients at risk of OSA and in patients with documented OSA may somewhat differ. Nevertheless, the implementation of ML bypasses this evolving debate by harnessing nonlinear dependencies between all useful variables.

From the events contemplated in the composite outcome variable, cardiogenic shock deserves special attention because it was the most frequent and had the steepest increase in incidence across OSA-risk categories. Cardiogenic shock represents a major issue because it represents a leading cause of in-hospital death in acute MI.[34] It was responsible for 60% of the deaths in our cohort, and its real prognostic significance might be underestimated, given the 6-month mortality variation that was observed in the SHOCK trial.[25]

The present study underlines ML applicability in any clinical area where large numbers of interrelated variables are available because traditional statistics, in general, areunable to exploit complex nonlinear dependencies. Further external validation of this model is clearly necessary to underpin its clinical consideration. Therein we believe that opting for high-sensitivity (ruling-out) performance threshold is in order as we explore the best ways to identify such patients who are at risk of individual events. From a clinical perspective, the present study triggers the question of whether a therapeutic approach to OSA or its risk components may improve short- and long-term clinical outcomes of patients with acute MI. This is yet to be clarified because secondary prevention studies in OSA have not demonstrated a clear benefit.[35,36] However, we suggest that benefit of evaluating OSA risk through the STOP-BANG questionnaire may arise from flagging a clinical profile that could benefit from more intense approaches to cardiovascular risk factors, such as obesity and lack of physical activity. Ad minimum, our results warrant improved monitorization of patients who are at risk of events during hospitalization because of acute MI.

Limitations

Our study is not without limitations. Most importantly, we did not have polysomnographic confirmation of OSA and it is not possible to determine whether the higher rate of cardiovascular outcomes is secondary to the combination of OSA risk factors or to OSA itself. Still, we used the STOP-BANG score as a surrogate marker of risk of adverse cardiovascular events rather than considering that OSA represents the mechanistic cause. On the methodologic side, our sample size could constrain the applicability of ML analytics. However, we undertook the following series of specific measures to guarantee the robustness of our results: first, resampling was performed in a five-fold cross-validation manner, which optimizes the use of the available cases and delivers a balanced overview of training and testing performance; second, the sample was well balanced (as prior published work has reported[17]) in terms of the outcome occurrence (also known as class-balance), which maximizes the possibility to obtain generalizable results; and third, the final set of features (seven variables) was discrete and robust, which minimizes the probability of dimensional overfitting. Additionally, we were not able to include an external validation sample to further test for accuracy generalizability. This exploratory complement represents the next logical step to undertake in this line of research. Finally, it may be possible that more severe cases could have been missed because of the screening intervals for patient inclusion (24 hours on average) that implies a discrete bias towards less serious cases. However, the rates of adverse outcomes were comparable, and in some instances, were higher than reported in other settings, which accounts for the representativity of the inclusion. As such, we acknowledge that our results must be understood contextually.

Interpretation

The integration of the STOP-BANG score into the clinical risk evaluation (considering Killip class, GRACE score, and simple laboratory values) of patients who are admitted for an acute MI through ML can optimize significantly the identification of patients who will experience an in-hospital cardiovascular event. An important proportion of patients in this setting demonstrate an intermediate- and high-risk of having OSA. The STOP-BANG score can aid in the integral risk stratification of patients with acute coronary syndromes. Further research into the evaluation of risk modification based on OSA assessment and the implementation of ML for complex variable integration is warranted.

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