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*Coronary Artery Disease*

# The Value of $CHA_2DS_2VASC$ Score in Predicting All-Cause Mortality in Patients with ST-Segment Elevation Myocardial Infarction Who Have Undergone Primary Percutaneous Coronary Intervention

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***Background:*** Acute coronary syndrome is the most common cause of cardiac morbidity and death. Various scoring systems have been developed in order to identify patients who are at risk for adverse outcome and may benefit from more aggressive and effective therapies.

***Objectives:*** This study was designed to evaluate the $CHA_2DS_2VASC$ score as a predictor of mortality inpatients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention (p-PCI).

***Methods:*** We evaluated 300 patients diagnosed with ST-elevation myocardial infarction who underwent p-PCI and calculated their $CHA_2DS_2VASC$ scores. According to their $CHA_2DS_2VASC$ scores, patients were divided into three groups. Group 1: 0-1 points (n = 101), Group 2: 2-3 points (n = 129), and Group 3: 4-9 points (n = 70). The mean, median and minimum duration of follow-up were $21.7 \pm 9.4$, 21, and 12 months, respectively. All-cause mortality was defined as the primary endpoint of the study.

***Results:*** All-cause mortality was 4% in Group 1, 8.5% in Group 2 and 27.1% in Group 3 respectively. Kaplan-Meier analysis showed that Group 3 ($CHA_2DS_2VASC \geq 4$) had a significantly higher incidence of death [p (log-rank) < 0.001]. In ROC analysis, AUC values for in hospital, 12-month and long-term mortality were 0.88 (0.77-0.99 95% CI), 0.82 (0.73-0.92 95% CI) and 0.79 (0.69-0.88 95% CI), respectively.

***Conclusions:*** $CHA_2DS_2VASC$ score can be used for predicting both in-hospital, 12-month and long-term mortality in patients with STEMI who have undergone p-PCI.

**Key Words:** $CHA_2DS_2VASC$ score • Primary percutaneous coronary intervention • ST segment elevation myocardial infarction

## INTRODUCTION

Acute coronary syndrome (ACS) is the most common cause of cardiac morbidity and death.[1] Accurate management decisions in light of comprehensive evaluations may improve the outcomes of patients at a higher risk. Various risk scores have been developed in order to identify patients at a higher risk of adverse outcomes who may benefit from more aggressive and effective therapies. Currently, the most widely used of these scores are Thrombolysis in Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE).[2,3] The $CHA_2DS_2VASC$ risk score was developed to predict

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the risk of stroke in patients with atrial fibrillation (AF).[4] This score includes variables such as heart failure, hypertension, age, diabetes mellitus, gender, vascular disease, and stroke. Since these components are also risk factors for atherosclerosis and ischemic heart disease, it may be reasonable to use this score for the risk stratification of ACS patients irrespective of AF.[5-8] The ease of calculation at the bedside means that this score is advantageous compared to others that require a computer. Therefore, this study aimed to investigate the value of $CHA_2DS_2VASC$ score in predicting in-hospital and long-term mortality in patients with ST-segment elevation myocardial infarction (STEMI) who had undergone a primary percutaneous intervention (p-PCI).

## METHODS

Three hundred patients who had undergone p-PCI for STEMI between 2012 and 2014 were enrolled. STEMI was diagnosed based on the presence of ST-segment elevation > 1 mm in two contiguous electrocardiographic leads, or with presumably new left bundle-branch block and chest pain exceeding 30 minutes. Baseline clinical and demographic characteristics as well as procedural data were obtained from hospital records. All patients above 18 years of age were included in the study, except for those with a history of cardiogenic shock, cardiac arrest, stage 4-5 chronic renal failure and treatment with thrombolytic agents. Before the procedure, all patients were treated with 300 mg of aspirin and a loading dose of 600 mg of clopidogrel. All p-PCI procedures were performed by experienced interventional cardiologists using the femoral approach. Patients undergoing p-PCI were given 100 IU/kg heparin during the procedure, which was reduced to 60 IU/kg if a glycoprotein IIb-IIIa inhibitor was administered. The use of glycoprotein IIb-IIIa inhibitors, thrombus aspiration, and stent selection were left to the operator's discretion. All patients signed an informed consent form. Ethical board approval was provided by the local ethics committee.

When calculating $CHA_2DS_2VASC$ scores, each factor including previous heart failure, hypertension, diabetes mellitus, vascular disease, female gender, and age between 65-74 years were given 1 point, whereas 2 points were given to an age above 75 years and a history of transient ischemic attack, stroke, or thromboembolic event. Since acute myocardial infarction (AMI) is considered to be a vascular disease, all patients with AMI received at least 1 point. According to their $CHA_2DS_2VASC$ score, the patients were divided into three groups: group 1: 0-1 points; group 2: 2-3 points; and group 3: 4-9 points. The mean, median and minimum follow-up periods were 21.7 $\pm$ 9.4, 21, and 12 months, respectively. All-cause mortality was defined as the primary endpoint of the study. The national death notification system and hospital records were used to obtain information on mortality.

### Statistical analysis

Statistical analysis was performed using SPSS software version 21 (SPSS Inc., Chicago, Illinois). Data were reported as means $\pm$ SDs for continuous variables. Categorical variables were reported as percentages, and continuous variables were compared among groups using one-way analysis of variance or the Kruskal-Wallis test. Categorical data were compared using the chi-square test. Event-free survival curves were generated using the Kaplan-Meier method, and differences in survival curves among the groups were assessed using the log-rank test. A p-value < 0.05 was considered to be statistically significant. Receiver operating characteristic (ROC) curves were generated to assess the sensitivity and specificity of the $CHA_2DS_2VASC$ score in predicting mortality. Pairwise comparisons of ROC curves were performed using the de-Long method (Medcalc version 16, free trial). "Goodness-of-fit" was evaluated using the Hosmer-Lemeshow test (p > 0.1 considered to indicate a lack of deviation between the model and observed event rates).

## RESULTS

The clinical, demographic and laboratory data of the patients in the three different groups are given in Table 1 and Table 2. There were significant differences among the groups in age, creatinine and glucose levels on admission and the frequencies of diabetes mellitus, hypertension, hyperlipidemia, previous coronary artery disease, previous myocardial infarction, previous AF, previous stroke, and history of heart failure. In addition, the incidence of current smoking, proportion of male sex, estimated glomerular filtration rate, and hemoglobin

**Table 1.** The clinical and demographic features of the study population according to $CHA_2DS_2VASC$ score

| | $CHA_2DS_2VASC$ = 1 (n = 101) | $CHA_2DS_2VASC$ = 2-3 (n = 129) | $CHA_2DS_2VASC \geq 4$ (n = 70) | p value |
|---|---|---|---|---|
| Age (years) | 50.4 ± 7.4 | 58.1 ± 9.2 | 72.6 ± 9.2 | < 0.001 |
| Male gender | 101 (100%) | 107 (82.9%) | 29 (41.4%) | < 0.001 |
| Diabetes mellitus | 0 (0%) | 40 (31%) | 37 (52.9%) | < 0.001 |
| Hypertension | 0 (0%) | 87 (67.4%) | 65 (92.9%) | < 0.001 |
| Hypercholesterolemia | 2 (2%) | 13 (10.2%) | 10 (10.5%) | 0.01 |
| Current smoking | 76 (75.2%) | 64 (49.6%) | 11 (15.7%) | < 0.001 |
| Previous MI | 2 (1.9%) | 10 (7.8%) | 9 (15.9%) | 0.02 |
| Previous stroke | 0 (0%) | 0 (0%) | 10 (14.3%) | < 0.001 |
| Previous CAD | 7 (6.9%) | 31 (24%) | 29 (41.4%) | < 0.001 |
| Previous AF | 2 (1.9%) | 1 (0.8%) | 3 (4.3%) | 0.23 |
| History of HF | 0 (0%) | 2 (1.5%) | 8 (11.4%) | < 0.001 |
| TIMI STEMI score | 1.4 ± 1.3 | 2.3 ± 1.4 | 4.7 ± 2.5 | < 0.001 |
| GRACE ACS score | 93.4 ± 13.1 | 107.5 ± 17.1 | 137.2 ± 17.8 | < 0.001 |
| In-hospital medication | | | | |
| Dual antiplatalet | 100 (99%) | 128 (99.2%) | 67 (97.1%) | 0.44 |
| Statin | 100 (99%) | 129 (100%) | 70 (100%) | 0.37 |
| β blocker | 101 (100%) | 127 (98.5%) | 69 (98.6%) | 0.46 |
| ACE-I/ARB | 70 (69.3%) | 108 (83.7%) | 60 (85.7%) | 0.009 |

ACS, acute coronary syndrome; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; AF, atrial fibrillation; CAD, coronary artery disease; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

**Table 2.** Biochemical characteristics of the study population according to $CHA_2DS_2VASC$ score

| | $CHA_2DS_2VASC$ = 1 (n = 101) | $CHA_2DS_2VASC$ = 2-3 (n = 129) | $CHA_2DS_2VASC \geq 4$ (n = 70) | p value |
|---|---|---|---|---|
| Serum glucose level on admission (mg/dL) | 110.2 ± 23.94 | 149.5 ± 69.4 | 170.6 ± 66.4 | < 0.001 |
| Creatinine level on admission (mg/dL) | 0.82 ± 0.16 | 0.86 ± 0.24 | 1.2 ± 1.1 | < 0.001 |
| eGFR (ml/min/1.73 $m^2$) | 107.6 ± 30.9 | 98.9 ± 31.1 | 72.9 ± 28.9 | < 0.001 |
| eGFR < 60 ml/min/1.73 $m^2$ | 3 (2.9%) | 11 (8.6%) | 22 (31.9%) | < 0.001 |
| Hemoglobin (gr/dL) | 14.5 ± 1.4 | 13.8 ± 1.9 | 12.3 ± 1.5 | < 0.001 |

eGFR, estimated glomerular filtration rate.

levels gradually decreased from those with a high (group 3) to low (group 1) $CHA_2DS_2VASC$ score.

The angiographic and procedural characteristics of the subjects in the three study groups are presented in Table 3. Drug-eluting stents (DES) were used less frequently and bare metal stents (BMS) were used more frequently in all patient groups. The incidence of DES implantation increased from group 1 to group 3. Myocardial infarction localization, infarct-related arteries and the rates of in-hospital coronary artery bypass graft surgery and staged PCI were similar between the groups.

The rates of in-hospital, 12-month and all-cause mortality in long-term follow-up are shown in Figures 1, 2, and 3, and were significantly higher in group 3 compared to the other two groups. In ROC analysis, area under the ROC curve (AUC) values for in-hospital, 12-month and all-cause mortality were 0.88 (0.77-0.99 95% CI), 0.82 (0.73-0.92 95% CI) and 0.79 (0.69-0.88 95% CI), respectively. The AUC values for TIMI STEMI score for in-hospital, 12-month and long-term mortality were 0.81 (0.65-0.97 95% CI), 0.80 (0.71-0.90 95% CI) and 0.81 (0.72-0.90 95% CI), respectively, and the AUC values for GRACE ACS score for in-hospital, 12-month and long-term mortality were 0.88 (0.77-0.98 95% CI), 0.76 (0.68-0.84 95% CI) and 0.73 (0.66-0.81 95% CI), respectively. A pairwise comparison of ROC curves showed that the predictive value of $CHA_2DS_2VASC$ risk score with regards to 12-month and long-term mortality were similar to the GRACE ACS and TIMI STEMI risk scores (using the de-Long method for 12-month mortality; $AUC_{chadsvasc}$ vs.

**Table 3.** Angiographic and procedural characteristics of the study population according to $CHA_2DS_2VASC$ score

| | $CHA_2DS_2VASC$ = 1 (n = 101) | $CHA_2DS_2VASC$ = 2-3 (n = 129) | $CHA_2DS_2VASC \geq 4$ (n = 70) | p value |
|---|---|---|---|---|
| Stent type | | | | < 0.001 |
| BMS | 76 (75.2%) | 89 (69%) | 36 (51.4%) | |
| DES | 15 (14.9%) | 31 (24%) | 15 (21.4%) | |
| BMS + DES | 8 (7.9 %) | 5 (3.9%) | 9 (12.8%) | |
| Balloon angioplasty only | 2 (2%) | 4 (3.1%) | 10 (14.3%) | |
| MI localization | | | | 0.73 |
| Anterior | 62 (61.4%) | 75 (59.1%) | 36 (52.9%) | |
| Inferior | 36 (35.6%) | 44 (34.6%) | 28 (41.2%) | |
| Inferolateral | 3 (3%) | 5 (3.9%) | 2 (2.9%) | |
| Posterior | 0 (0%) | 2 (1.6%) | 2 (2.9%) | |
| High lateral | 0 (0%) | 1 (0.8%) | 0 (0%) | |
| Infarct related artery | | | | 0.71 |
| LAD | 62 (61.4%) | 76 (60.3%) | 36 (55.4%) | |
| LCX | 13 (12.9%) | 19 (15.1%) | 7 (10.8%) | |
| RCA | 26 (25.7%) | 29 (23%) | 22 (33.8%) | |
| Saphenous graft | 0 (0%) | 2 (1.2%) | 0 (0%) | |
| CABG or staged PCI in-hospital | 18 (17.8%) | 34 (26.4%) | 21 (30%) | 0.15 |

BMS, bare metal stent; CABG, coronary artery by-pass graft; DES, drug eluting stent; LAD, left anterior descending artery; LCX, left circumflex artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

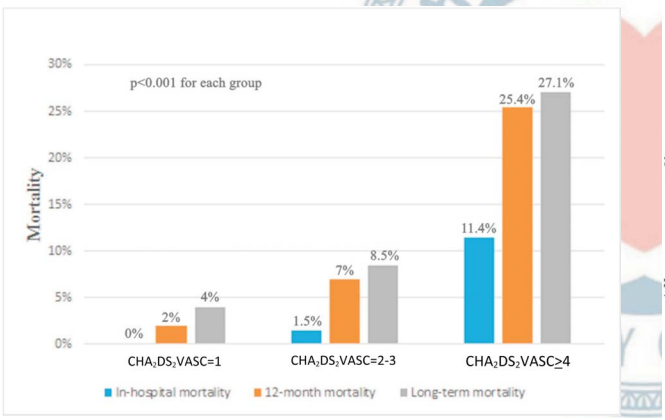


***Figure 1.*** *Rates of in-hospital, 12-month and long-term mortality according to the $CHA_2DS_2VASC$ score.*

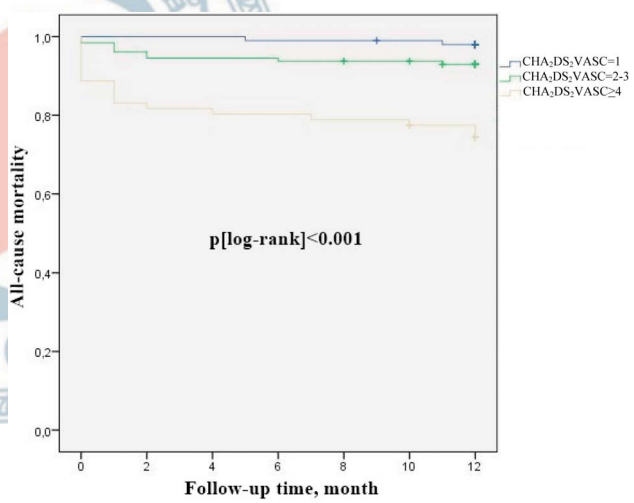


***Figure 2.*** *Kaplan-Meier curves for 12-month mortality.*

$AUC_{grace}$ z test = 1.23 p = 0.22, $AUC_{chadsvasc}$ vs. $AUC_{timi\ stemi}$ z test = 0.32 p = 0.75, $AUC_{grace\ acs}$ vs. $AUC_{timi\ stemi}$ z test = 0.85 p = 0.39; for long-term mortality $AUC_{chadsvasc}$ vs. $AUC_{grace\ acs}$ z test = 1.25 p = 0.21, $AUC_{chadsvasc}$ vs. $AUC_{timi\ stemi}$ z test = 0.29 p = 0.77, $AUC_{grace\ acs}$ vs. $AUC_{timi\ stemi}$ z test = 1.47 p = 0.14) (Figure 4).

The Hosmer-Lemeshow test (TIMI STEMI, p = 0.88; GRACE ACS, p = 0.08; $CHA_2DS_2VASC$, p = 0.59) demonstrated that the calibrations of these three risk scores to predict adverse events were accurate.

## DISCUSSION

The results of this study suggest that the $CHA_2DS_2$-VASC score can be used to predict both in-hospital and long-term mortality in patients with STEMI who have undergone a p-PCI, which is currently the treatment of choice. Despite advances in reperfusion therapies, STEMI is still a significant cause of morbidity and mortality.[9] It is necessary to identify high-risk patients by risk stratifi-

cation to both define a treatment strategy and manage potential long-term problems. In this respect, STEMI presents a unique picture representing the patients at highest risk who require emergency interventions.

The $CHA_2DS_2VASC$ score was initially developed for stroke risk stratification in patients with AF. However, it has recently been applied to different clinical conditions. For example, it has been used to estimate the risk of stroke and the development of thromboembolism in-patients with heart failure who are in sinus rhythm. It has also been used to estimate the risk of stroke following bypass surgery and stroke without AF in the general population.[10-12] Although the prediction of mortality is not the primary aim of the $CHA_2DS_2VASC$ score, its components such as older age, diabetes mellitus, heart failure, and prior vascular disease are all important prognostic factors for STEMI.[9,13-17] Therefore, various studies have investigated its prognostic value in ACS.[5-8] Other non-ACS studies have also suggested an increase in mortality in parallel with an increase in risk score.[10,12]

In our study, patients in group 3 ($CHA_2DS_2VASC$ score $\geq 4$) were associated with a statistically significantly greater incidence of in-hospital and long-term mortality during long-term follow-up compared to those with a lower $CHA_2DS_2VASC$ score. Although the positive predictive value was low (11.4% for in-hospital and 27% for long-term mortality), the negative predictive value was high (99.1% for in-hospital and 93.5% for long-term mortality). The patients in group 3 were also associated with a worse clinical status, such as older age, higher incidence of diabetes mellitus, impaired renal function and left ventricular dysfunction, which may explain the higher mortality rate.

Huang et al. evaluated patients AMI according to their $CHADS_2$ score, and found that the group with a high $CHADS_2$ score had a statistically significantly greater incidence of the primary endpoints (all-cause mortality, myocardial infarction, and cerebrovascular events) during 1 and 3 years of follow-up compared to the groups with low and medium scores.[6] They also found that the $CHADS_2$ score was an independent predictor of future major adverse cardiovascular events in patients with AMI, and therefore suggested that the $CHADS_2$ score was superior to the TIMI score and equivalent to the GRACE score in predicting long-term adverse events. However, they did not report the number of patients with STEMI or the number of patients treated with p-PCI. In addition, the rate of in-hospital revascularization gradually decreased from the patients with a low to high $CHADS_2$ score, and the total revascularization rate was around 60% which seems quite low.

Similarly, a study that included over 15,000 patients

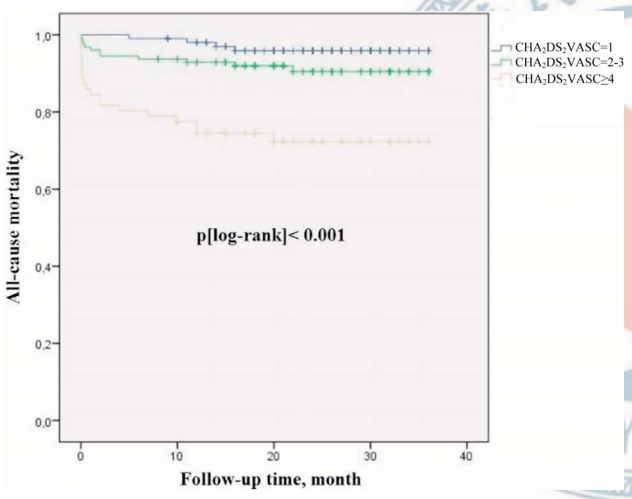


***Figure 3.*** *Kaplan-Meier curves for all-cause mortality in long-term follow-up.*

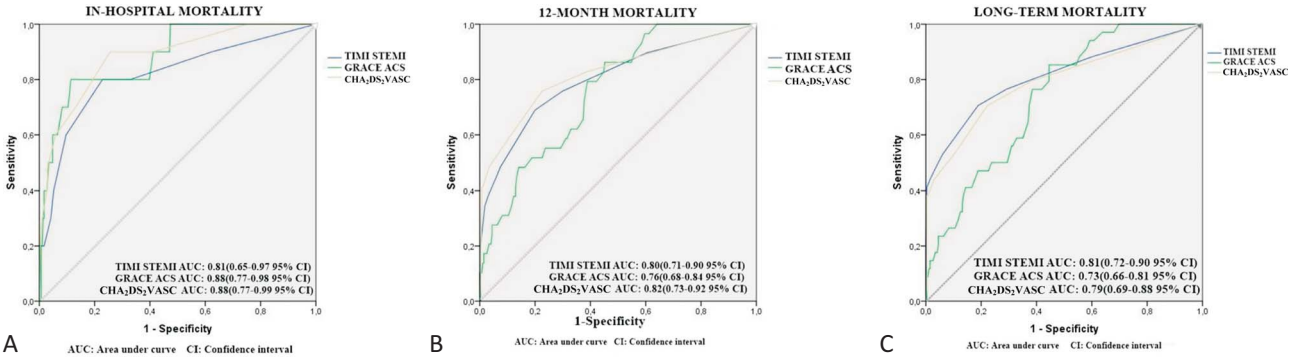


***Figure 4.*** *ROC curves comparing $CHA_2DS_2VASC$, TIMI STEMI and GRACE ACS risk scores for in-hospital, 12-month and long-term mortality.*

hospitalized for AMI reported that as the $CHA_2DS_2VASC$ score increased, the incidence of cardiac events was also higher inlong-term follow-up.[7] The authors did not identify any differences in terms of in-hospital events, however they reported that the $CHA_2DS_2VASC$ score may be superior to the TIMI and $CHADS_2$ scores and equivalent to the GRACE score in predicting long-term adverse events. They also suggested that the $CHA_2DS_2$-VASC score may be a more important predictor of STEMI than non-ST segment elevation myocardial infarction. However, the study included patients who had not only undergone p-PCI but also thrombolysis, and those managed conservatively in the STEMI group. Moreover, they did not give any information regarding the stent types used in the STEMI group.

Likewise, Chua et al. conducted a study of 3,183 patients with ACS to investigate the value of $CHA_2DS_2VASC$ score in predicting prognosis.[8] They demonstrated that a high $CHA_2DS_2VASC$ score was a predictor of all major adverse cardiovascular events in patients with AMI. They also reported that the $CHA_2DS_2VASC$ score was superior to the $CHADS_2$ score in predicting cardiac events. However, they did not analyze STEMI patients who underwent p-PCI separately.

Our findings are consistent with the current literature, in that the discriminatory performance of the $CHA_2DS_2VASC$ score was equivalent to the TIMI STEMI and GRACE ACS risk scores in both in-hospital and long-term mortality. It seems that a $CHA_2DS_2VASC$ score $\geq 4$ serves as a cut off point above which mortality significantly increases. Despite a low positive predictive value, a score of < 4 had a good negative predictive ability, which may indicate low in-hospital and long-term mortality (99.1% for in-hospital and 93.5% for long-term mortality).

### Limitations

This study has a number of limitations. Although it is a single center and retrospective study, a real-world, unselected population was investigated. The endpoints of the study were in-hospital and long-term all-cause mortality, however, we did not include major adverse cardiac events such as repeated myocardial infarction, hospitalization and revascularization. In addition, we mainly used BMS for implantation and only clopidogrel as an adenosine diphosphate receptor antagonist due to financial considerations.

## CONCLUSIONS

In conclusion, the $CHA_2DS_2VASC$ score can be used in patients who have undergone p-PCI to predict both in-hospital and long-term mortality. This may lead to the optimization of therapies and reduce the risk of subsequent adverse events.

## ACKNOWLEDGMENTS

None.

## CONFLICTS OF INTEREST

All the authors declare no conflict of interest.

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