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# The Association between Vitamin D Levels and Thrombus Burden in Patients with ST-Elevation Myocardial Infarction

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## Abstract

***Background:*** *In current practice, establishing the potential predictors of high thrombus burden (HTB) before primary percutaneous coronary intervention (PCI) is crucial for its management. In this research, we aimed to investigate the association between vitamin D levels and HTB in patients with ST-elevation myocardial infarction (STEMI).*

***Methods:*** *This prospective, observational study was conducted on 257 STEMI patients undergoing primary PCI in Van Education and Research Hospital between March 2020 and March 2021. The thrombus burden grade was determined for each subject. The study population was divided into 2 groups: patients with HTB and those with low thrombus burden (LTB) based on the thrombus burden grade. Demographic, laboratory, and angiographic features were compared between the groups.*

***Results:*** *In total, 154 patients (mean age±SD=63.42±11.53 y, 65.6% male) had HTB and 103 patients had LTB (mean age±SD=61.50±10.23 y, 70.9% male). The patients stratified into the HTB group had lower vitamin D levels than those in the LTB group (8.0 ng/mL vs 17.9 ng/mL, respectively; P<0.001). The patients with HTB and low vitamin D levels had lower post-PCI thrombolysis in myocardial infarction (TIMI) flow, TIMI myocardial perfusion grade, and post-PCI ST resolution. In a multivariable analysis, vitamin D was an independent predictor of HTB among the STEMI patients (OR: 0.76, 95%CI: 0.70–0.82; P<0.001). The ideal value of vitamin D to predict HTB was >17.6 ng/mL with a sensitivity of 81.8% and a specificity of 90.3%.*

***Conclusion:*** *The study results showed that vitamin D levels were an independent predictor of HTB in STEMI patients treated by primary PCI.*

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***Keywords:*** *Coronary thrombosis; Vitamin D; ST elevation myocardial infarction*

## Introduction

In current practice, vitamin D deficiency is a continuing major health problem worldwide with a high prevalence.[1] A deficiency in vitamin D can result from a limited cutaneous synthesis due to the lack of sun exposure and an insufficient dietary intake. Current evidence suggests that vitamin D deficiency affects not only the musculoskeletal system but also the cardiovascular system. Moreover, recent studies have revealed an inverse relationship between vitamin D

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levels and coronary artery disease.[2, 3] It has been considered that the impairment of endothelial function, the upregulation of the renin-angiotensin system,[4-6] the inflammation of cardiomyocytes by monocyte and macrophages,[7, 8] vascular calcification, and the impairment of arterial stiffness[9] are possible underlying mechanisms of this association.

Primary percutaneous coronary intervention (PCI) is the best treatment option for ST-elevation myocardial infarction (STEMI) according to the recent STEMI guideline.[10] Although significant improvements have been achieved in primary PCI procedures, high thrombus burden (HTB) remains a prominent risk factor for adverse events, including stent thrombosis, no-reflow, distal embolization, and increased mortality.[11-13] Hence, establishing the potential predictors of HTB before primary PCI is crucial for its management. Accordingly, this study aimed to investigate whether there was a correlation between vitamin D levels and coronary artery thrombus burden in patients with STEMI undergoing primary PCI.

## *Methods*

A total of 257 STEMI patients who underwent primary PCI in Van Education and Research Hospital between March 2020 and March 2021 were recruited for this prospective, observational study. The exclusion criteria were as follows: vitamin D supplementation therapy in the preceding 3 months, an acute infection, hematologic disease, active malignancy, known parathyroid diseases, and grades IV and V chronic renal disease or undergoing hemodialysis or peritoneal dialysis. The baseline characteristics and detailed medical and family histories of all the patients were noted.

All blood samples were collected upon admission to the emergency department. Blood samples of vitamin D and parathyroid hormone (PTH) were centrifuged and stored at −70 °C until studied. A UniCel DxI800 Immunoassay Analyzer (Beckman Coulter Inc, Brea, CA, USA) and an Immulite 2000 Model Analyzer (Siemens Healthcare GmbH, Henkestr, Erlangen, Germany) were used to measure vitamin D and PTH levels, respectively. Other blood parameters were analyzed using either a Beckman Coulter LH 780 Hematology Analyzer (Beckman Coulter, FL, USA) or a Beckman Coulter LH 780 Device.

According to the operator's discretion, standard coronary angiography was performed through either the transradial approach or the transfemoral approach using the standard Judkins methods. All the patients were medicated with 300 mg of acetylsalicylic acid and a loading dose of $P_2Y_{12}$ inhibitors on admission before the coronary angiography procedure. The decision to use glycoprotein IIb/IIIa receptor inhibitors was left to the attending cardiologist's discretion. The primary PCI procedure was performed according to the recommendations of an updated STEMI guideline.[10] The angiographic images of the patients were carefully analyzed by 2 experienced operators who were blinded to all clinical parameters. Angiographic thrombus burden was graded as follows: grade 0: no thrombus, grade I: possible thrombus (reduced contrast density, haziness, and irregular lesion contour), grade II: the greatest dimension of the thrombus being less than half the vessel diameter, grade III: the greatest dimension of the thrombus ranging between half and twice the vessel diameter, grade IV: the greatest dimension of the thrombus being twice the vessel diameter, and grade V: total vessel occlusion by the thrombus.[14] The patients were grouped into low thrombus burden (LTB) (grades I–III) and HTB groups (grades IV and V) based on the final thrombus score.[15] The thrombolysis in myocardial infarction (TIMI) flow was assessed immediately following the primary PCI procedure using the TIMI flow grade classification.[16] The TIMI myocardial perfusion grade (TMPG) was categorized as follows: no myocardial blush as grade 0, minimal myocardial blush as grade I; moderate myocardial blush as grade II; and normal myocardial blush as grade III.[17] The TIMI flow grades 0, I, and II were considered no-reflow. ST-segment resolution on electrocardiography was evaluated at the 90th minute, and a resolution of above 70% was considered successful, whereas 70% and less ST resolution was the criterion of electrocardiographic no-reflow.

The STEMI diagnosis was made based on the following diagnostic criteria: 1) ST-segment elevation ( ≥2.5 mm in men <40 years, ≥2 mm in men >40 years or ≥1.5 mm in women in leads $V_2$–$V_3$ or ≥1 mm in the absence of left ventricular hypertrophy or left bundle branch block in at least 2 contiguous leads), 2) prolonged typical chest pain (>30 min), and 3) elevation of serum biomarkers of myocardial damage above the 99th percentile upper limit.[18] Hypertension was described as a systolic pressure of 140 mmHg or greater and/or a diastolic pressure of 90 mmHg or greater in at least 2 measurements or the current use of antihypertensive agents. Diabetes mellitus was defined as the use of antidiabetic agents or a fasting glucose level of 126 mg/dL or higher or a postprandial glucose level of 200 mg/dL or higher. Cigarette smoking was defined as patients who had smoked for more than 6 months during the past year. Family history of coronary artery disease was defined as a history of this disease in first-degree relatives (<55 y for men and <65 y for women). Vitamin D deficiency was described as a vitamin D level of less than 20 ng/mL.

All the statistical analyses were performed on SAS University Edition, version 9.04 (SAS/STAT, SAS Institute Inc, NC, USA). To test the normality of the data, we utilized the Kolmogorov–Smirnov test. Continuous variables with a normal distribution were presented as the mean ± the standard deviation, while those without a normal distribution were presented as the median (interquartile range [IQ]). Categorical variables were expressed as numbers and percentages (%). The independent Student *t*

test or the Mann–Whitney *U* test was used to compare the continuous variables between the groups as appropriate. The categorical variables were compared using the Pearson $\chi^2$ test or the Fisher exact test between the groups. A univariable logistic regression analysis was performed to identify the association between predictors and HTB. Variables with statistical significance in the univariable logistic regression were entered into a multivariable logistic regression model to detect the independent predictors of HTB. A receiver operating characteristic (ROC) curve analysis was plotted to determine the cutoff value of vitamin D via the Youden index method, and the area under the curve (AUC) was gained. A P value of less than 0.05 was considered significant in all the statistical analyses.

## Results

The distribution of the study population (n=257 cases, mean age=62.11±12.27 y) was as follows: 154 patients (59.9% of the study population, mean age [SD]=63.42 [11.53], 65.6% male) in the HTB group and 103 patients (40.1% of the study

Table 1. Comparison of the demographic features and laboratory data of all the patients according to thrombus burden*

| Variables | High Thrombus Burden (n=154) | Low Thrombus Burden (n=103) | P |
|---|---|---|---|
| Age, (y) | 63.42±11.53 | 61.50±10.23 | 0.186 |
| Sex, (male) | 101 (65.6) | 73 (70.9) | 0.374 |
| History | | | |
| Diabetes mellitus | 36 (23.4) | 20 (19.4) | 0.451 |
| Hypertension | 64 (41.6) | 35 (34.0) | 0.221 |
| Cigarette smoking | 65 (42.2) | 49 (47.6) | 0.396 |
| Vascular disease | 3 (1.9) | 2 (1.9) | 1.000 |
| Previous history of CAD | 26 (16.9) | 16 (15.5) | 0.774 |
| Family history of CAD | 48 (31.2) | 27 (26.2) | 0.392 |
| Systolic blood pressure, (mmHg) | 120 (117.5-130) | 130 (120-130) | 0.139 |
| Heart rate, (beat/min) | 85.5 (78-92.5) | 85 (75-90) | 0.103 |
| Laboratory Results | | | |
| CRP, (mg/dL) | 3.50±2-60 | 2.30±2-3.10 | 0.001 |
| Albumin, (g/dL) | 4 (3.1-4.2) | 4.1 (3.8-4.3) | 0.001 |
| White blood cell count, ($x10^3$/mL) | 10.3 (8.9-12.8) | 9.6 (7.7-10.7) | <0.001 |
| Hemoglobin, (g/dL) | 14.7 (13.6-15.6) | 15 (14-15.8) | 0.230 |
| Neutrophil, ($x10^3$/mL) | 7.9 (6.3-9.8) | 6.2 (4.9-7.6) | <0.001 |
| Lymphocyte, ($x10^3$/mL) | 1.8 (1.3-2.3) | 2.1 (1.5-2.6) | 0.019 |
| Platelet count, ($x10^3$/mL) | 230 (192-257) | 214 (182-265) | 0.372 |
| Cardiac troponin I, (mg/L) | 2.3 (0.2-12.3) | 0.3 (0.1-2.2) | <0.001 |
| Total cholesterol, (mg/dL) | 176 (143-202) | 161 (145-198) | 0.302 |
| LDL cholesterol, (mg/dL) | 111.53±35.24 | 104.31±33.93 | 0.103 |
| HDL cholesterol, (mg/dL) | 39 (32-42) | 38 (33-44) | 0.222 |
| Triglyceride, (mg/dL) | 94 (75-136) | 110 (78-201) | 0.027 |
| Creatinine, (mg/dL) | 1 (0.8-1) | 0.9 (0.8-1) | 0.079 |
| Vitamin D, (ng/mL) | 8 (5.6-10.5) | 17.9 (14.6-24) | <0.001 |
| Parathyroid hormone, (pg/mL) | 45 (28-60) | 36 (23-47) | 0.001 |
| Calcium, (mg/dL) | 8.9 (8.8-9) | 9 (8.9-9) | 0.202 |
| Left ventricular EF, (%) | 45 (40-45) | 50 (45-55) | <0.001 |
| Previous Medications | | | |
| Antiplatelet | 7 (4.6) | 8 (7.8) | 0.291 |
| Aspirin | 28 (18.2) | 22 (21.4) | 0.528 |
| Statin | 21 (13.6) | 19 (18.5) | 0.297 |
| ACE inhibitors/ARB | 32 (20.8) | 23 (22.3) | 0.766 |
| Beta-blocker | 25 (16.2) | 20 (19.4) | 0.511 |

*Data are presented as mean±SD, median ($IQ_{25\%-75\%}$), or n (%)

CAD, Coronary artery disease; CRP, C-reactive protein; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; EF, Ejection fraction; ACE, Angiotensin-converting enzyme; ARB, Angiotensin-receptor blocker

population, mean age [SD=61.50 [10.23], 70.9% male) in the LTB group (Table 1). There were no significant differences between the HTB and LTB groups with respect to age, sex, comorbid diseases, and previous medications. Patients in the HTB group had higher C-reactive protein (CRP), white blood cell (WBC) counts, neutrophils, and cardiac troponin I, as well as lower albumin, lymphocytes, triglycerides, and left ventricular ejection fraction (EF) than those in the LTB group. Vitamin D levels were significantly lower in the HTB group (8 ng/mL vs 17.9 ng/mL, respectively; P<0.001). Additionally, PTH was significantly higher in the HTB group (45 pg/mL vs 36 pg/mL, respectively; P<0.001).

The angiographic findings of all the cases are summarized in Table 2. The pain-to-balloon time and the door-to-balloon time were longer in the HTB group than in the LTB group. As expected, the patients included in the HTB group had a significantly higher Killip status (>II), distal embolization, and no-reflow. The corrected TIMI frame count (cTFC) was longer in the HTB group than in the LTB group. The patients stratified into the HTB group had lower post-TIMI flow, TMPG, and ST-resolution than those in the LTB group.

As shown in Table 3, we also compared angiographic findings of all the patients according to vitamin D levels (patients with vitamin D ≤20 ng/mL and patients with vitamin D >20 ng/mL). The prevalence of vitamin D deficiency in the STEMI patients was 80.9% (n=208 cases). Infarct-related artery (IRA) lesion length, IRA cTFC, and the pain-to-balloon time were longer in the vitamin D deficiency group. The triple-vessel lesion was more commonly observed in the vitamin D deficiency group. Additionally, patients who had a vitamin D deficiency had a higher rate of HTB and lower rates of post-PCI-TIMI flow, TMPG, and post-PCI ST resolution after the procedure.

The univariable and multivariable logistic regression results are shown in Table 4. CRP, albumin, the WBC count, neutrophils, cardiac troponin I, the left ventricular EF, the pain-to-balloon time, PTH, and vitamin D were associated with HTB in the univariable regression. These parameters were entered into a multivariable logistic regression analysis. According to this analysis, albumin, neutrophils, cardiac

Table 2. Comparison of the angiographic data of all the cases according to thrombus burden*

| | High Thrombus Burden (n=154) | Low Thrombus Burden (n=103) | P |
|---|---|---|---|
| Infarct-Related Artery | | | 0.824 |
| LAD | 70 (45.4) | 49 (47.6) | |
| Cx | 32 (20.8) | 23 (22.3) | |
| RCA | 52 (33.8) | 31 (30.1) | |
| Number of Diseased Vessels | | | 0.418 |
| Single-vessel | 98 (68.0) | 78 (75.0) | |
| Double-vessel | 25 (17.4) | 16 (15.4) | |
| Triple-vessel | 21 (14.6) | 10 (9.6) | |
| IRA vessel diameter (≥4 mm) | 13 (8.4) | 7 (6.8) | 0.813 |
| IRA lesion length, (mm) | 26 (20-36) | 24 (20-30) | 0.236 |
| Pain-to-balloon time, (min) | 300 (180-480) | 185 (130-360) | 0.014 |
| Door-to-balloon time, (min) | 45 (40-60) | 40 (30-60) | 0.032 |
| Killip class II-IV | 49 (31.8) | 20 (19.4) | 0.027 |
| Postprocedural TIMI flow ≥ III | 134 (87.0) | 99 (96.1) | 0.014 |
| TMPG ≥ II | 72 (46.8) | 72 (69.9) | <0.001 |
| Procedure | | | <0.001 |
| Direct stenting | 12 (7.8) | 41 (39.8) | |
| PTCA+stenting | 137 (88.9) | 60 (58.3) | |
| Only PTCA | 5 (3.3) | 2 (1.9) | |
| IRA cTFC, (frames/second) | 18 (14-30) | 12 (11-13) | <0.001 |
| ≥70% ST resolution in ECG | 79 (51.3) | 95 (92.2) | <0.001 |
| Distal embolization | 7 (4.6) | 0 (0.0) | 0.044 |
| No-reflow | 20 (13.0) | 4 (3.9) | 0.014 |

*Data are presented as median ($IQ_{25\%-75\%}$), or n (%)
LAD, Left anterior descending; Cx, Circumflex artery; RCA, Right coronary artery; IRA, Infarct-related artery; TIMI, Thrombolysis in myocardial infarction; TMPG, TIMI myocardial perfusion grade; PTCA, Percutaneous transluminal coronary angioplasty; cTFC, Corrected TIMI frame count; ECG, Electrocardiography

Table 3. Comparison of the angiographic data of all the cases based on vitamin D levels*

| | Vitamin D | | P |
|---|---|---|---|
| | ≤ 20 (n=208) | > 20 (n=49) | |
| Infarct-Related Artery | | | 0.956 |
| LAD | 97 (46.6) | 24 (48.9) | |
| Cx | 66 (31.8) | 15 (30.6) | |
| RCA | 45 (21.6) | 10 (20.5) | |
| Number of Diseased Vessels | | | 0.016 |
| Single-vessel | 120 (57.7) | 39 (79.6) | |
| Double-vessel | 43 (20.7) | 6 (12.2) | |
| Triple-vessel | 45 (21.6) | 4 (8.2) | |
| IRA vessel diameter ≥4 mm | 16 (7.7) | 3 (6.1) | 1.000 |
| IRA lesion length, (mm) | 26 (22-38) | 23 (18-26) | 0.001 |
| Pain-to-balloon time, (min) | 250 (180-420) | 180 (120-240) | 0.007 |
| Door-to-balloon time, (min) | 45 (35-60) | 40 (30-60) | 0.061 |
| Killip class II-IV | 57 (27.7) | 10 (20.4) | 0.368 |
| Postprocedural TIMI flow ≥III | 184 (88.5) | 49 (100) | 0.011 |
| TMPG ≥II | 111 (53.4) | 34 (69.4) | 0.042 |
| Procedure | | | 0.026 |
| Direct stenting | 36 (17.3) | 17 (34.7) | |
| PTCA+stenting | 166 (79.8) | 31 (63.3) | |
| Only PTCA | 6 (2.9) | 1 (2.0) | |
| ≥ 70% ST resolution in ECG | 131 (63.6) | 43 (87.8) | 0.001 |
| IRA cTFC, (frames/second) | 15 (12-29) | 13 (11-13) | <0.001 |
| High thrombus burden grade ≥4 | 148 (71.2) | 6 (12.2) | <0.001 |
| Distal embolization | 5 (2.4) | 0 (0.0) | 0.586 |
| No-reflow | 24 (11.5) | 0 (0.0) | 0.011 |

*Data are presented as median ($IQ_{25\%-75\%}$), or n (%)
LAD, Left anterior descending; Cx, Circumflex artery; RCA, Right coronary artery; IRA, Infarct-related artery; TIMI, Thrombolysis in myocardial infarction; TMPG, TIMI myocardial perfusion grade; PTCA, Percutaneous transluminal coronary angioplasty; cTFC, Corrected TIMI frame count; ECG, Electrocardiography

Table 4. Univariable and multivariable logistic regression analysis for predicting high thrombus burden

| | Univariable OR (95%CI) | P | Multivariable OR (95%CI) | P |
|---|---|---|---|---|
| CRP, (mg/dL) | 1.24 (1.01-1.43) | 0.001 | 1.14 (0.96-1.39) | 0.154 |
| Albumin, (g/dL) | 0.67 (0.46-0.95) | 0.029 | 0.37 (0.19-0.68) | 0.002 |
| WBC, ($x10^3$/mL) | 1.21 (1.10-1.34) | <0.001 | 0.89 (0.70-1.12) | 0.325 |
| Neutrophil, ($x10^3$/mL) | 1.33 (1.19-1.50) | <0.001 | 1.26 (0.99-1.64) | 0.065 |
| Lymphocyte, ($x10^3$/mL) | 1.00 (0.99-1.13) | 0.626 | - | - |
| Cardiac troponin I, (mg/L) | 1.10 (1.06-1.15) | <0.001 | 1.09 (1.02-1.18) | 0.019 |
| Triglyceride, (mg/dL) | 1.00 (0.99-1.00) | 0.175 | - | - |
| Vitamin D, (ng/mL) | 0.75 (0.70-0.80) | <0.001 | 0.76 (0.70-0.82) | <0.001 |
| PTH, (pg/mL) | 1.02 (1.01-1.03) | 0.011 | 1.02 (1.00-1.04) | 0.067 |
| Left ventricular EF, (%) | 0.91 (0.87-0.94) | <0.001 | 0.92 (0.86-0.97) | 0.003 |
| Pain-to-balloon time, (min) | 1.00 (1.00-1.00) | 0.007 | 1.00 (1.00-1.01) | 0.017 |

OR, Odds ratio; CI, Confidence interval; CRP, C-reactive protein; WBC, White blood cell; PTH, Parathyroid hormone; EF, Ejection fraction

troponin I, the left ventricular EF, the pain-to-balloon time, and vitamin D levels were independent predictors of HTB (Figure 1). A ROC curve analysis showed that the ideal value of vitamin D to predict HTB was >17.6 with a sensitivity of 81.8% and a specificity of 90.3% (Figure 2).

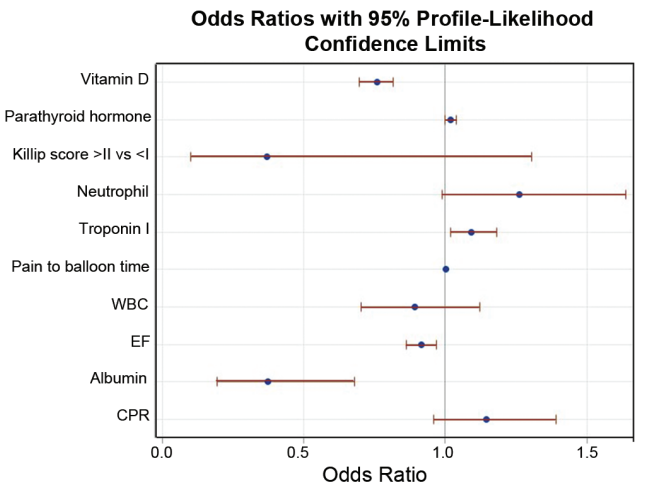


Figure 1. Independent predictors for high thrombus burden
WBC, White blood cell; EF, Ejection fraction; CRP, C-reactive protein

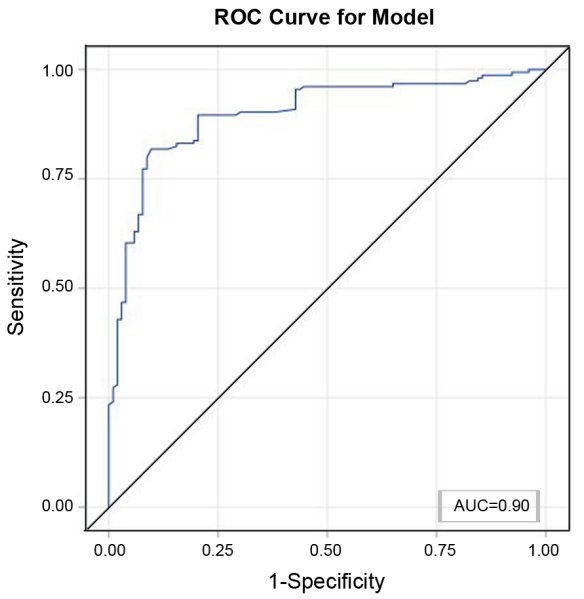


Figure 2. Receiver operating characteristics (ROC) curve analysis of the vitamin D level in predicting high thrombus burden

## Discussion

The main findings of this research could be summarized as follows: 1) vitamin D levels were significantly lower in HTB patients, 2) patients with low vitamin D levels had lower post-PCI-TIMI flow, TMPG, and post-PCI ST resolution after the procedure, and 3) vitamin D was an independent predictor of HTB in STEMI patients treated with primary PCI.

The partial or total occlusion of the coronary artery by an intracoronary thrombus following an acute plaque rupture is the main mechanism of acute MI.[19] Hence, rapid restoration of the coronary flow and improving myocardial reperfusion are the main goals of primary PCI in patients with STEMI. However, the presence of an intracoronary thrombus and the quantity of this thrombus are shown to be linked with adverse cardiovascular events, including distal embolization, no-reflow, and stent thrombosis following primary PCI in STEMI patients.[11, 12] A prior study demonstrated that the presence of HTB was a strong predictor of 30-day mortality among these patients.[11] Thus, establishing the potential predictors of HTB before primary PCI is crucial to its management.

Vitamin D is a lipophilic hormone that is mainly presented in 2 forms: vitamin D2 and vitamin D3. The human body cannot synthesize vitamin D2; therefore, it must be taken from dietary sources.[20] Vitamin D3, which is also known as cholecalciferol, can be produced in the skin through the ultraviolet irradiation of 7-dehydrocholesterol. Vitamin D3 and vitamin D2 are then converted into 25(OH) vitamin D3 and 25(OH) vitamin D2 in the liver by an enzyme 25-hydroxylase, respectively.[21] Notably, 25(OH) vitamin D encompasses both 25(OH) vitamin D3 and 25(OH) vitamin D2, and it reflects the vitamin D status in the human body.[22] A vitamin D level of less than 20 ng/mL is considered vitamin D deficiency in clinical practice. Vitamin D binds to the vitamin D binding protein (VDR), which is distributed in various cells, including cardiac, endothelial, and vascular smooth cells, to be transferred to the vital organs.[23] The antithrombotic effects of vitamin D have been demonstrated in the current literature.[24, 25] These antithrombotic effects of vitamin D are considered due to the actions of VDR ligands.[26] Supporting these findings, a prior experimental study conducted on rats revealed that platelet aggregation was upregulated and the gene expression of anti-thrombin and thrombomodulin in the aorta, liver, and kidneys was reduced, while tissue factor expression in the liver and kidney was enhanced in VDR knockout rats.[27] Furthermore, VDR may have a critical role in the coagulation pathway by activating the tissue factor-mediated mechanism and connecting the pathways of the coagulation cascade.[28, 29]

Platelets with a larger size have been shown to be more aggressive and have a higher pro-thrombotic ability. To support this finding, a higher mean platelet volume was demonstrated to be linked with a higher risk of deep vein thrombosis and acute MI in a previous study.[30] The mean platelet volume was inversely correlated with vitamin D levels in patients with stable coronary artery disease,[25] which might imply one of the underlying linkages between vitamin

D and coronary artery disease. The uptake of cholesterol by macrophages converts them into foam cells, which deposit in the endothelium and promote atherosclerosis by forming atheromatous plaques.[31] However, vitamin D inhibits this uptake and plays an anti-atherogenic role in the human body. A positive correlation between vitamin D levels and high-density lipoprotein and apolipoprotein A-1 and a negative correlation between low-density lipoprotein and triglyceride have been noted in the literature, which might explain the possible mechanisms between vitamin D deficiency and atherosclerosis.[32] On the other hand, HTB has also been linked to endothelial dysfunction,[33] and studies have revealed that low vitamin D levels enhance endothelial dysfunction.[34, 35]

The importance of vitamin D levels has been investigated in patients with coronary artery disease and acute coronary syndrome. In a prior study, vitamin D deficiency was associated with a higher prevalence of triple-vessel coronary artery disease, which is compatible with our study results.[36] Roy et al[37] found that vitamin D deficiency was related to an increased risk of acute MI despite the adjustment of other possible risk factors. The prevalence of vitamin D deficiency was found higher in patients with STEMI and vitamin D was associated with worse outcomes in STEMI patients in several studies.[2, 38, 39]

In the literature, there is no solid evidence about whether vitamin D levels are independently related to HTB or no-reflow. It has been reported that STEMI patients who developed no-reflow had lower levels of vitamin D than those with normal flow.[40] Nonetheless, vitamin D levels were not found to be an independent predictor of no-reflow according to the multivariate analysis in that study. Abdallah et al[41] investigated the association between vitamin D levels and thrombus burden in STEMI patients. Nevertheless, they failed to achieve a significant difference between the low vitamin D group and the control group with respect to thrombus burden, TIMI flow, and the frequency of no-reflow. They only noted that the low vitamin D group had worse TMPG than the control group, concordant with our study results. It seems possible that their results might be due to a small sample size of the study relative to our study (n=80). In the present study, we grouped our study population as a vitamin D deficiency group (<20 ng/mL) and a control group (>20 ng/mL) as described in the literature. We found that vitamin D deficiency was prevalent among STEMI patients, and it was associated with HTB in those patients. Because STEMI is one of the major causes of mortality and morbidity worldwide and the thrombus burden is related to adverse events in STEMI, early detection and successful treatment of vitamin D deficiency might be beneficial to prevent adverse events in such patients.

The major limitation of this study was the relatively small sample size. Another limitation was that the research was conducted at a single center in which vitamin D deficiency was more prevalent. In this study, we could not follow up the patients after hospital discharge. Therefore, the data on long-term mortality were unknown. A lack of more sensitive and specific methods for detecting intracoronary thrombi and myocardial perfusion such as intravascular ultrasonography, optical coherence tomography, and cardiac magnetic resonance imaging was another limitation. Finally, our results should be confirmed in further prospective studies with a large sample size.

## Conclusion

This research concluded that vitamin D levels were lower in STEMI patients with high thrombus burden. In addition, a low vitamin D level was an independent predictor of high thrombus burden in patients with STEMI undergoing primary PCI.

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