

# The Association Between Blood Pressure and Coronary Plaque Morphology

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## Article

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# Abstract

## Background

Hypertension is a major determinant of coronary artery disease and is closely associated with coronary artery calcification. However, the underlying mechanisms have been underexplored, and the relationship between blood pressure (BP) and plaque morphology has not been thoroughly investigated.

## Methods

In this retrospective multicenter study, 293 patients undergoing optical coherence tomography (OCT)-guided percutaneous coronary intervention were enrolled. Patients were categorized according to the stage of hypertension and tertiles of systolic BP (SBP) and diastolic BP (DBP). Detailed OCT-guided qualitative plaque characteristics, including calcification, lipid components, and features of plaque vulnerability, were evaluated. Multivariable generalized linear models were used to assess the associations between BP parameters and OCT findings after adjustment for clinical confounders.

## Results

The stages of hypertension were associated with a greater maximal calcium arc. Both SBP and DBP were associated with a greater maximal calcification arc. In contrast, BP parameters were not consistently associated with OCT-defined features of plaque vulnerability, including thin-cap fibroatheroma and lipid-rich plaque. The association between BP and coronary calcification was more pronounced in patients presenting with acute coronary syndrome than in those with chronic coronary syndrome. These relationships remained significant after multivariable adjustment.

## Conclusion

Both SBP and DBP were associated with more significant coronary calcification rather than vulnerable plaque features.

## Introduction

Hypertension, one of the most pervasive cardiovascular risk factors worldwide, contributes to coronary artery disease (CAD) through sustained mechanical and biochemical injury to the arterial wall.<sup>1</sup> Elevated blood pressure (BP) promotes endothelial dysfunction, oxidative stress, and maladaptive vascular remodeling, all of which contribute to accelerated atherogenesis.<sup>2,3</sup> The cardiovascular risk rises continuously across the BP spectrum, even below traditional diagnostic thresholds, and emphasizes the

cumulative BP burden as a major determinant of vascular injury.<sup>4</sup> Despite these insights, the microscopic structural consequences of BP elevation within coronary plaques remain poorly understood.

Coronary artery calcification (CAC), widely evaluated using computed tomography (CT), is a robust marker of the cumulative atherosclerotic burden and future cardiovascular risk<sup>5,6</sup> Optical coherence tomography (OCT), with microscopic resolution, enables the detailed visualization of calcification that is strongly associated with the procedural complexity of percutaneous coronary intervention (PCI) and worse clinical outcomes<sup>7–11</sup> Although prior studies have shown that systolic BP (SBP) is a major determinant of coronary calcium progression<sup>1,4</sup>, they did not provide evidence relevant to the microscopic plaque morphology.<sup>1,4</sup> In this study, we aimed to investigate the association of hypertension with OCT-defined plaque morphology.

## Results

### Baseline Characteristics

The median age of the study population was 70 years, and 235 patients (80.2%) were male. The median systolic BP (SBP) was 130 mmHg, and the median diastolic BP (DBP) was 76 mmHg (Table 1).

Table 1  
Baseline characteristics

| Age, median (IQR), years                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | All (n = 293)    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 70 (65–76)       |
| Women, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 58 (19.8)        |
| Body mass index, median (IQR), kg/m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 23.8 (21.8–26.1) |
| Clinical presentation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |
| Acute coronary syndromes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 66 (22.5)        |
| Chronic coronary syndrome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 227 (77.5)       |
| Risk factors, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                  |
| Hypertension                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 229 (78.2)       |
| Hyperlipidemia                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 206 (70.3)       |
| Diabetes mellitus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 141 (48.1)       |
| Chronic kidney disease                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 47 (16.0)        |
| Current smoker                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 36 (12.3)        |
| AF, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 31 (10.6)        |
| prior PCI, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 143 (48.8)       |
| Prior CABG, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 11 (3.8)         |
| History of ACS, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 93 (31.7)        |
| Laboratory data                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                  |
| LDL-C, median (IQR), mg/dL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 88 (66–109)      |
| HDL-C, median (IQR), mg/dL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 48 (41–55)       |
| Triglyceride, median (IQR), mg/dL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 113 (81–160)     |
| HbA1c, median (IQR), %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 6.3 (5.8–7.0)    |
| eGFR, median (IQR), mL/min/1.73 m <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 68.9 (57.6–78.1) |
| Medication before PCI, No (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                  |
| Data are given as n (%), mean ± SD or median (IQR). ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; CABG, Coronary artery bypass grafting; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCI, percutaneous coronary intervention; P2Y12, purinergic receptor type Y, subtype 12. |                  |

| Age, median (IQR), years                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | All (n = 293) |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 70 (65–76)    |
| P2Y12 inhibitor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 230 (78.5)    |
| Aspirin                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 226 (77.1)    |
| ACEi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 53 (18.1)     |
| ARB                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 117 (39.9)    |
| ARNI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 26 (8.9)      |
| β-blocker                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 125 (42.7)    |
| Statin                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 234 (79.9)    |
| DOAC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 31 (10.6)     |
| Warfarin                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 5 (1.7)       |
| Data are given as n (%), mean ± SD or median (IQR). ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; CABG, Coronary artery bypass grafting; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCI, percutaneous coronary intervention; P2Y12, purinergic receptor type Y, subtype 12. |               |

## OCT Findings According to Hypertension Stage

The patients were divided into three groups according to the stages of hypertension. As the hypertension stage increased, the maximal calcification arc became greater (normotensive vs. stage 1 vs. stage 2: 69° vs. 110° vs. 144°;  $p$  for trend < 0.001), and the proportion of target lesions with a calcium score  $\geq 3$  also increased (normotensive vs. stage 1 vs. stage 2: 18.4% vs. 26.2% vs. 36.4%;  $p$  for trend = 0.003) (Fig. 1). The other OCT findings are summarized in Table 2. Conversely, the prevalence of lipid-rich plaques and ruptured plaques decreased in patients with higher hypertension stages. (normotensive vs. stage 1 vs. stage 2: 86.4% vs. 75% vs. 68.3%;  $p$  for trend = 0.001) The association between hypertension stage and maximal calcium arc was more evident in ACS than in CCS (Supplemental Table 1).

Table 2  
Other OCT findings and SBP

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Hypertension           |                              |                             |         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------------|-----------------------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Normotensive (n = 125) | Stage 1 (n = 80)             | Stage 2 (n = 88)            | p value |
| <i>Qualitative analysis, No (%)</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                        |                              |                             |         |
| TCFA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 41 (32.8)              | 19 (23.8)                    | 19 (21.6)                   | 0.144   |
| Lipid-rich plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 108 (86.4)             | 60 (75.0)                    | 60 (68.2) <sup>a</sup>      | 0.005   |
| Macrophage                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 92 (73.6)              | 59 (73.8)                    | 65 (73.9)                   | 0.999   |
| Microvessels                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 72 (57.6)              | 38 (47.5)                    | 42 (47.7)                   | 0.239   |
| Cholesterol crystal                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 48 (38.4)              | 35 (43.8)                    | 34 (38.6)                   | 0.715   |
| Layered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 77 (61.6)              | 47 (58.8)                    | 49 (55.7)                   | 0.687   |
| Multilayered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 21 (16.8)              | 4 (5.0) <sup>a</sup>         | 11 (12.5)                   | 0.043   |
| Thrombus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 24 (19.2)              | 12 (15.0)                    | 9 (10.2)                    | 0.201   |
| Ruptured plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 29 (23.2)              | 9 (11.2)                     | 6 (6.8) <sup>a</sup>        | 0.002   |
| Calcium score $\geq 3$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 23 (18.4)              | 21 (26.2)                    | 32 (36.4) <sup>a</sup>      | 0.013   |
| <i>Quantitative analysis</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                        |                              |                             |         |
| Maximal lipid arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 230 (156–360)          | 206 (107–283)                | 206 (72–292)                | 0.085   |
| Maximal calcification arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 69 (24–120)            | 110 (43–186) <sup>a</sup>    | 144 (59–238) <sup>a</sup>   | < 0.001 |
| Maximal layer arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 139 (0–236)            | 94 (0–192)                   | 112 (0–206)                 | 0.276   |
| Lipid index,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1358 (518–2734)        | 1063 (199–2068) <sup>a</sup> | 944 (141–2100)              | 0.064   |
| Calcium index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 219 (25–795)           | 487 (94–1827) <sup>a</sup>   | 700 (169–1800) <sup>a</sup> | < 0.001 |
| <p>Patients were divided into three groups based on the blood pressure as follows: normotensive (SBP &lt; 130 mmHg and DBP &lt; 80 mmHg), Stage 1 hypertension (SBP 130–139 mmHg or DBP 80–89 mmHg) and Stage 2 hypertension (SBP <math>\geq</math> 140 mmHg or DBP <math>\geq</math> 90 mmHg). The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> &lt; 0.05 vs normotensive group; <sup>b</sup> indicates <i>p</i> &lt; 0.05 vs stage 1 hypertension group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma.</p> |                        |                              |                             |         |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Hypertension           |                  |                  |         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------|------------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Normotensive (n = 125) | Stage 1 (n = 80) | Stage 2 (n = 88) | p value |
| Layer index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 553 (0-1249)           | 241 (0-905)      | 378 (0-1644)     | 0.293   |
| Macrophage grade                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 8 (0–17)               | 6 (0–17)         | 6 (0–14)         | 0.721   |
| MLA, mm <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1.4 (1.1–1.9)          | 1.5 (1.0-1.9)    | 1.3 (0.9–1.7)    | 0.378   |
| Area stenosis, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 76.9 (71.1–83.0)       | 74.0 (67.4–83.3) | 77.5 (69.3–81.7) | 0.380   |
| <p>Patients were divided into three groups based on the blood pressure as follows: normotensive (SBP &lt; 130 mmHg and DBP &lt; 80 mmHg), Stage 1 hypertension (SBP 130–139 mmHg or DBP 80–89 mmHg) and Stage 2 hypertension (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg). The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> &lt; 0.05 vs normotensive group; <sup>b</sup> indicates <i>p</i> &lt; 0.05 vs stage 1 hypertension group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma.</p> |                        |                  |                  |         |

Table 3  
Other OCT findings and DBP

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | SBP             |                      |                              |         |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|----------------------|------------------------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Low (n = 93)    | Moderate (n = 100)   | High (n = 100)               | p value |
| <i>Qualitative analysis, No (%)</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                 |                      |                              |         |
| TCFA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 31 (33.3)       | 29 (29.0)            | 19 (19.0)                    | 0.069   |
| Lipid-rich plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 79 (84.9)       | 82 (82.0)            | 67 (67.0) <sup>a, b</sup>    | 0.005   |
| Macrophage                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 69 (74.2)       | 77 (77.0)            | 70 (70.0)                    | 0.527   |
| Microvessels                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 49 (52.7)       | 57 (57.0)            | 46 (46.0)                    | 0.292   |
| Cholesterol crystal                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 39 (41.9)       | 43 (43.0)            | 35 (35.0)                    | 0.458   |
| Layered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 60 (64.5)       | 57 (57.0)            | 56 (56.0)                    | 0.426   |
| Multilayered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 18 (19.4)       | 7 (7.0) <sup>a</sup> | 11 (11.0)                    | 0.029   |
| Thrombus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 18 (19.4)       | 17 (17.0)            | 10 (10.0)                    | 0.169   |
| Ruptured plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 21 (22.6)       | 16 (16.0)            | 7 (7.0) <sup>a</sup>         | 0.010   |
| Calcium score $\geq 3$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 16 (17.2)       | 23 (23.0)            | 35 (35.0) <sup>a</sup>       | 0.014   |
| <i>Quantitative analysis</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                 |                      |                              |         |
| Maximal lipid arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 230 (134–360)   | 220 (157–331)        | 183 (72–288)                 | 0.022   |
| Maximal calcification arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 75 (26–117)     | 90 (32–166)          | 145 (65–242) <sup>a, b</sup> | < 0.001 |
| Maximal layer arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 155 (0–226)     | 0 (0–213)            | 115 (0–206)                  | 0.257   |
| Lipid index,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1436 (436–2824) | 1221 (507–2179)      | 811 (141–1982)               | 0.050   |
| Calcium index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 246 (38–779)    | 341 (49–1161)        | 959 (207–1898) <sup>a</sup>  | 0.004   |
| Layer index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 675 (0–1290)    | 0 (0–1100)           | 327 (0–1348)                 | 0.630   |
| Macrophage grade                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 8 (2–17)        | 7 (2–18)             | 5 (0–13)                     | 0.297   |
| <p>Patients were divided into three groups based on the tertiles of systolic blood pressure (SBP) as follows: Low: &lt; 120 mmHg; Moderate: 120–135 mmHg; and High &gt; 135 mmHg. The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> &lt; 0.05 vs Low group; <sup>b</sup> indicates <i>p</i> &lt; 0.05 vs Moderate group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma.</p> |                 |                      |                              |         |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | SBP              |                    |                  |                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|--------------------|------------------|----------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Low (n = 93)     | Moderate (n = 100) | High (n = 100)   | <i>p</i> value |
| MLA, mm <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1.5 (1.1–1.9)    | 1.4 (1.0-1.9)      | 1.3 (1.0-1.8)    | 0.668          |
| Area stenosis, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 77.3 (72.2–82.2) | 77.3 (68.4–84.1)   | 75.2 (67.2–81.0) | 0.040          |
| <p>Patients were divided into three groups based on the tertiles of systolic blood pressure (SBP) as follows: Low: &lt; 120 mmHg; Moderate: 120–135 mmHg; and High &gt; 135 mmHg. The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> &lt; 0.05 vs Low group; <sup>b</sup> indicates <i>p</i> &lt; 0.05 vs Moderate group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma.</p> |                  |                    |                  |                |

Table 4  
OCT findings according to diastolic blood pressure tertiles

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | DBP             |                   |                           | <i>p</i> value |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-------------------|---------------------------|----------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Low (n = 97)    | Moderate (n = 90) | High (n = 106)            |                |
| <i>Qualitative analysis, No (%)</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                 |                   |                           |                |
| TCFA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 32 (33.0)       | 25 (27.8)         | 22 (20.8)                 | 0.143          |
| Lipid-rich plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 81 (83.5)       | 71 (78.9)         | 76 (71.7)                 | 0.124          |
| Macrophage                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 69 (71.1)       | 67 (74.4)         | 80 (75.5)                 | 0.768          |
| Microvessels                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 53 (54.6)       | 50 (55.6)         | 49 (46.2)                 | 0.343          |
| Cholesterol crystal                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 35 (36.1)       | 35 (38.9)         | 47 (44.3)                 | 0.473          |
| Layered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 61 (62.9)       | 52 (57.8)         | 60 (56.6)                 | 0.634          |
| Multilayered plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 16 (16.5)       | 11 (12.2)         | 9 (8.5)                   | 0.222          |
| Thrombus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 17 (17.5)       | 15 (16.7)         | 13 (12.3)                 | 0.535          |
| Ruptured plaque                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 19 (19.6)       | 17 (18.9)         | 8 (7.5) <sup>a</sup>      | 0.026          |
| Calcium score ≥ 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 20 (20.6)       | 21 (23.3)         | 33 (31.1)                 | 0.200          |
| <i>Quantitative analysis</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                 |                   |                           |                |
| Maximal lipid arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 237 (136–360)   | 213 (122–315)     | 196 (80–293)              | 0.108          |
| Maximal calcification arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 68 (26–119)     | 106 (50–176)      | 128 (52–209) <sup>a</sup> | 0.010          |
| Maximal layer arc, °                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 139 (0-234)     | 107 (0-207)       | 110 (0-200)               | 0.283          |
| Lipid index,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1384 (430–2551) | 1207 (351–2559)   | 964 (189–2019)            | 0.299          |
| Calcium index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 246 (38–892)    | 536 (103–1761)    | 613 (120–1608)            | 0.193          |
| Layer index                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 537 (0-1221)    | 322 (0-1267)      | 304 (0-983)               | 0.781          |
| Macrophage grade                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 8 (0–13)        | 8 (1–22)          | 5 (1–13)                  | 0.799          |
| MLA, mm <sup>2</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1.4 (1.0-1.9)   | 1.5 (1.0-1.9)     | 1.3 (1.0-1.8)             | 0.716          |
| Patients were divided into three groups based on the tertiles of diastolic blood pressure (DBP) as follows: Low: < 73 mmHg; Moderate: 73–83; High: > 83 mmHg. The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> < 0.05 vs Low group; <sup>b</sup> indicates <i>p</i> < 0.05 vs Moderate group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma. |                 |                   |                           |                |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | DBP              |                   |                  |         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-------------------|------------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Low (n = 97)     | Moderate (n = 90) | High (n = 106)   | p value |
| Area stenosis, %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 76.3 (71.1–82.5) | 77.1 (68.6–82.5)  | 76.6 (67.4–83.1) | 0.194   |
| <p>Patients were divided into three groups based on the tertiles of diastolic blood pressure (DBP) as follows: Low: &lt; 73 mmHg; Moderate: 73–83; High: &gt; 83 mmHg. The <i>p</i> values were calculated by chi-square test for categorical variables or Mann-Whitney test for continuous variables. Tukey's honestly significant difference test was used for multiple comparisons. <sup>a</sup> indicates <i>p</i> &lt; 0.05 vs Low group; <sup>b</sup> indicates <i>p</i> &lt; 0.05 vs Moderate group. MLA, minimum lumen area; TCFA, thin-cap fibroatheroma.</p> |                  |                   |                  |         |

## OCT Findings According to Blood Pressure

The patients were divided into tertiles of SBP (low < 120 mmHg; moderate 120–135 mmHg; or high > 135 mmHg) and DBP (low < 73 mmHg; moderate 73–83 mmHg; or high > 83 mmHg). The maximal calcification arc increased with higher SBP (low vs moderate vs high: 75° vs 90° vs 140°; *p* for trend < 0.001) and with higher DBP (low vs moderate vs high: 68° vs 106° vs 128°; *p* for trend = 0.007) (Fig. 2). The prevalence of lesions with a calcium score ≥ 3 also increased with higher SBP (low vs moderate vs high: 17.2% vs 23.0% vs 35.0%; *p* for trend = 0.004) and showed a similar tendency with higher DBP (low vs moderate vs high: 20.6% vs 23.3% vs 31.1%; *p* for trend = 0.083) (Fig. 3). The maximal lipid arc was inversely correlated with the SBP. The associations of SBP with a smaller minimum lumen area and a greater percent area stenosis were evident in ACS, but not in CCS (Supplemental Table 2). DBP was associated with the maximal calcium arc only in ACS (Supplemental Table 3).

## Multivariable Analyses

Univariable and multivariable analyses demonstrated the significant associations of hypertension stages, SBP, or DBP with maximal calcification arc after adjustment for confounders (Supplemental Table 4 and Table 5).

Table 5

Multivariable associations between blood pressure parameters and OCT-derived calcification indices

| Variables                                                                                                                                                                                                                                                                                                                                                                                          | Univariable |              |                | Multivariable |              |                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|--------------|----------------|---------------|--------------|----------------|
|                                                                                                                                                                                                                                                                                                                                                                                                    | $\beta$     | 95% CI       | <i>p</i> value | $\beta$       | 95% CI       | <i>p</i> value |
| Hypertension Stages                                                                                                                                                                                                                                                                                                                                                                                | 27.96       | 13.30, 42.62 | < 0.001        | 24.35         | 9.541, 39.16 | 0.001          |
| Systolic blood pressure, per 1 tertile increment                                                                                                                                                                                                                                                                                                                                                   | 30.76       | 15.57, 45.95 | < 0.001        | 27.45         | 11.99, 42.91 | 0.001          |
| Diastolic blood pressure, per 1 tertile increment                                                                                                                                                                                                                                                                                                                                                  | 19.90       | 4.866, 34.94 | 0.010          | 21.55         | 7.032, 36.07 | 0.004          |
| A generalized linear model with identity links was conducted for the associations of hypertension stages, SBP or DBP with maximal calcification arc. Multivariable models included Age > 75 years, gender, clinical presentations, comorbidities (diabetes mellitus, hypertension, atrial fibrillation, Hb < 11g/dL), and treatment (SGLT2 inhibitor, Calcium channel blocker, ARB, ARNI, statin). |             |              |                |               |              |                |

## Discussion

The current study demonstrated the following: 1) the hypertension stage was associated with more significant coronary calcification; 2) both SBP and DBP showed associations with the maximal calcium arc and calcium score; 3) these associations were particularly pronounced in patients who presented with ACS, whereas SBP demonstrated a more consistent relationship across both ACS and CCS. These results suggest that BP may be reflected in OCT-detected calcium morphology, whereas the OCT features of plaque vulnerability were not significantly influenced by the BP parameters.

Previous population-based studies have shown that SBP is a critical determinant of the CAC progression measured by CT, even within the BP ranges previously considered to be normal.<sup>12</sup> However, CT is limited to evaluating coronary calcification and cannot resolve subclinical microscopic plaque structures. OCT overcomes this limitation by visualizing fine-scale calcium morphology, fibrous-cap thickness, and lipid accumulation.<sup>8,11,20</sup> In this context, the present OCT-guided findings are consistent with prior CT-based observations, supporting the concept that elevated BP is associated with increased coronary calcification even at a microstructural level. Notably, OCT did not demonstrate a strong or consistent association between BP parameters and the features of plaque vulnerability, such as TCFA or lipid-rich plaque. Although calcification is considered to take place in the region surrounding the necrotic core,<sup>21</sup> these results suggest that BP-related hemodynamic stress preferentially contributes to calcific plaque remodeling rather than to the fibrous-cap or lipid-core alterations typically associated with plaque vulnerability. This highlights the potential of OCT-detected calcification as an imaging marker of the cumulative BP burden in patients undergoing coronary intervention. Dietary interventions may reportedly induce plaque regression in normotensive but not hypertensive patients.<sup>22</sup> Although the BP fluctuates

over short periods, our findings support the concept that BP contributes to cumulative calcific remodeling, reinforcing the potential importance of appropriate BP control.<sup>23</sup>

The clinical relevance of these findings is underscored by the fact that only 54% of adults with hypertension are diagnosed, 42% receive treatment, and a mere 21% have their hypertension controlled.<sup>24</sup> Even stage 1 hypertension may be associated with measurable calcification, highlighting that early lifestyle modification and timely pharmacologic intervention could be beneficial.

The biological mechanisms linking BP to calcification are supported by experimental and clinical data. The sustained mechanical stress from elevated SBP and DBP may induce endothelial dysfunction and oxidative injury, which can trigger phenotypic modulation of the vascular smooth muscle cells toward osteoblastic states<sup>25,26</sup>. Mechanical stretching stimulates the release of matrix vesicles, which act as a nidus for microcalcification. Given that coronary calcification is thought to evolve from early microcalcifications that subsequently coalesce into sheet-like calcification as the plaques mature and stabilize, the present findings imply that elevated BP may promote calcification progression without necessarily enhancing vulnerable plaque formation. A study described a bidirectional vicious cycle in which hypertension promotes vascular calcification, which, in turn, exacerbates arterial stiffness and afterload, perpetuating further BP elevation.<sup>27</sup> This framework aligns with our findings showing robust associations between BP parameters and coronary calcification, indicating that coronary calcification assessment, such as the CAC score, may provide additional insights into BP-related vascular remodeling and help identify patients with a higher cumulative BP burden.

## Limitations

This study has certain limitations. First, the retrospective and cross-sectional design prevents causal inference, and bidirectional interactions, such as arterial stiffening contributing to higher SBP—cannot be excluded<sup>27</sup>. Second, the BP was measured at a single time point in the catheterization laboratory; ambulatory BP monitoring and long-term BP variability, both emphasized in the recent guidelines<sup>4,28</sup>, were not available. Third, although this was a multicenter study, the cohort consisted predominantly of Japanese patients, and race- or ethnicity-specific analyses were not performed, which may limit the generalizability of the findings to other populations. Fourth, although OCT offers superior spatial resolution, attenuation artifacts may have influenced the calcium measurements in lipid-rich plaques. Fifth, the medication use varied across hypertension stages, and residual confounding from antihypertensive therapy is possible. Sixth, the cohort consisted of patients undergoing PCI, which may limit the generalizability to lower-risk populations. Finally, the biomarkers of mineral metabolism, inflammation, and extracellular matrix remodeling were not assessed, preventing deeper mechanistic exploration.

## Conclusion

BP was associated with the extent of coronary calcification, whereas its relationship with OCT-defined features of plaque vulnerability was not evident in this cohort. Even Stage 1 hypertension was associated with measurable calcific changes, emphasizing the need for early and rigorous BP control. Prospective studies incorporating longitudinal BP assessment and mechanistic biomarkers are needed to determine whether aggressive BP management can slow coronary calcification.

## Methods

### Study participants

In this study, we adopted a multicenter, retrospective, cross-sectional design. Patients who had undergone OCT before PCI were enrolled. The study included patients diagnosed with chronic coronary syndrome (CCS) or acute coronary syndrome (ACS) from August 2019 to September 2024. The patient data were extracted from the ongoing “Yamagata OCT Registry.” The data were collected from five institutions in Japan: the Japanese Red Cross Ishinomaki Hospital, Okitama Public General Hospital, Nihonkai General Hospital, Yamagata Prefectural Central Hospital, and Yamagata University Hospital. For analysis, all OCT images and clinical data were obtained from the five centers and forwarded to the cardiovascular imaging laboratory at Yamagata University School of Medicine (Yamagata, Japan).

Of these 412 patients, 48 with in-stent restenosis, 39 with poor OCT quality, and 32 with hemodialysis were excluded. Ultimately, 293 patients were enrolled in this study. The site investigators determined the culprit vessel based on clinical and angiographic information and/or left ventricular regional wall motion abnormalities. In cases of multivessel disease in which the culprit vessel was not apparent, the choice was made based on the lesions showing evidence of recent plaque disruption in patients presenting with ACS or the most severe lesion in those with CCS. All the selected lesions were subsequently confirmed using OCT.

All procedures were performed in accordance with the ethical, institutional, and/or national research committee guidelines of the centers at which the studies were conducted, and complied with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Institutional Ethics Committee of the Yamagata University School of Medicine (approval no. 2022-17). Written informed consent was obtained from all the participants or waived by the institutional review board, owing to the retrospective nature of the study.

### OCT Image Acquisition and Analysis

All OCT datasets were analyzed offline by three independent investigators blinded to clinical information, using a dedicated review workstation (LightLab Imaging Inc.). Both qualitative and quantitative assessments of plaque morphology were performed as previously described.<sup>12</sup> A layered plaque was defined as a lesion showing one or more distinct layers with differing optical densities, clearly demarcated from the underlying plaque structure. The length of the layered component was measured longitudinally. The layer index, representing the volumetric extent of the layered structure, was calculated

as the mean layer arc multiplied by the layer length.<sup>13</sup> Thin-cap fibroatheroma (TCFA) was defined as a plaque with a maximal lipid arc > 90 ° and thinnest fibrous cap thickness < 65 µm.<sup>12</sup> Macrophage accumulation was defined as the presence of highly backscattering focal granular regions.<sup>12</sup> The degree of macrophage accumulation was graded as follows: grade 0, no macrophage; grade 1, localized macrophage accumulation; grade 2, clustered accumulation < 1 quadrant; grade 3, clustered accumulation ≥ 1 quadrant but < 3 quadrants; and grade 4, clustered accumulation ≥ 3 quadrants. Grading was performed every 1 mm along the entire target plaque, and the summation of 0 to 4 grades was calculated.<sup>14</sup> Lipid was defined as a signal-poor region with a diffuse border, and the degree of lipid arc was measured at 1 mm intervals.<sup>12</sup> The lipid length was obtained on the longitudinal view, and the lipid index was calculated as the product of the mean lipid arc and lipid length.<sup>15</sup> Lipid-rich plaque was defined as a plaque with a maximal lipid arc > 90 °.<sup>12</sup> Microvessels were defined as the presence of signal-poor structures with vesicular or tubular shapes.<sup>12</sup> Cholesterol crystals were identified as thin and linear regions of high signal intensity with high backscattering within a plaque.<sup>12</sup> Calcification was defined as a signal-poor or heterogeneous region with a sharply delineated border.<sup>12</sup>

## Measurement of BP

BP was measured in the supine position at the bedside prior to PCI. The patients were categorized by BP as follows: normotensive (SBP < 130 mmHg and DBP < 80 mmHg), stage 1 hypertension (SBP 130–139 mmHg or DBP 80–89 mmHg), and stage 2 hypertension (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg).<sup>16</sup>

## Statistical Analysis

Continuous variables with a normal distribution were expressed as mean ± SD, whereas the median (interquartile range [25th–75th percentile]) was used for nonnormally distributed variables. In comparing the patient baseline characteristics, normally distributed variables were compared using the Student's t-test, whereas nonnormally distributed variables were compared using the Mann–Whitney U test. Categorical data were expressed as absolute frequencies and percentages and compared using the  $\chi^2$  test or Fisher's exact test, as appropriate. The *p* for trend was calculated using the Jonckheere–Terpstra test for continuous dependent variables or Cochran–Armitage test for categorical variables. Tukey's honestly significant difference test was used for multiple comparisons. Multiplicative interaction terms were used to calculate the statistical significance of the interaction between the clinical presentation and hypertension stage and between the clinical presentation and the BP tertiles group. In a multivariable regression analysis, the impacts of BP tertile groups on the OCT features of vulnerability were identified by a generalized linear model with identity link (continuous dependent variable) adjusting for confounders including age, sex, clinical presentations, comorbidities (diabetes mellitus, hypertension, atrial fibrillation, hemoglobinlevel < 11g/dL), and treatment (SGLT2 inhibitor, Calcium blocker, ARB, ARNI, statin), which were selected based on previous studies.<sup>17–19</sup> For all tests, a two-sided *p*-value < 0.05 was considered statistically significant. Statistical analyses were performed using R software, version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). One author had full access to all the data in the study and took responsibility for the integrity of the data and accuracy of the data analysis.

# Abbreviations

BP = blood pressure

SBP = systolic blood pressure

DBP = diastolic blood pressure

OCT = optical coherence tomography

CAC = coronary artery calcification

TCFA = thin-cap fibroatheroma

# Declarations

## Acknowledgments:

We thank the staff of the participating institutions for their assistance with data collection and OCT image acquisition.

## Author contributions:

IT and KD had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: KD.

Acquisition, analysis, or interpretation of data: OY, GJ, MT, KT, TT, KS, HH, DH, KS, ST, OK, NT, YT, SS, FA, WT, WM.

Drafting of the manuscript: IT, KD.

Critical revision of the manuscript for important intellectual content: NT, YT, SS, FA, WT, WM.

Statistical analysis: IT and KD.

Administrative, technical, or material support: OY, GJ, MT, and WM.

Supervision: WT and WM.

## Data Availability Statement:

The corresponding author's data supporting this study's findings are available upon reasonable request.

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**Declaration of generative AI use:** None

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## Figures

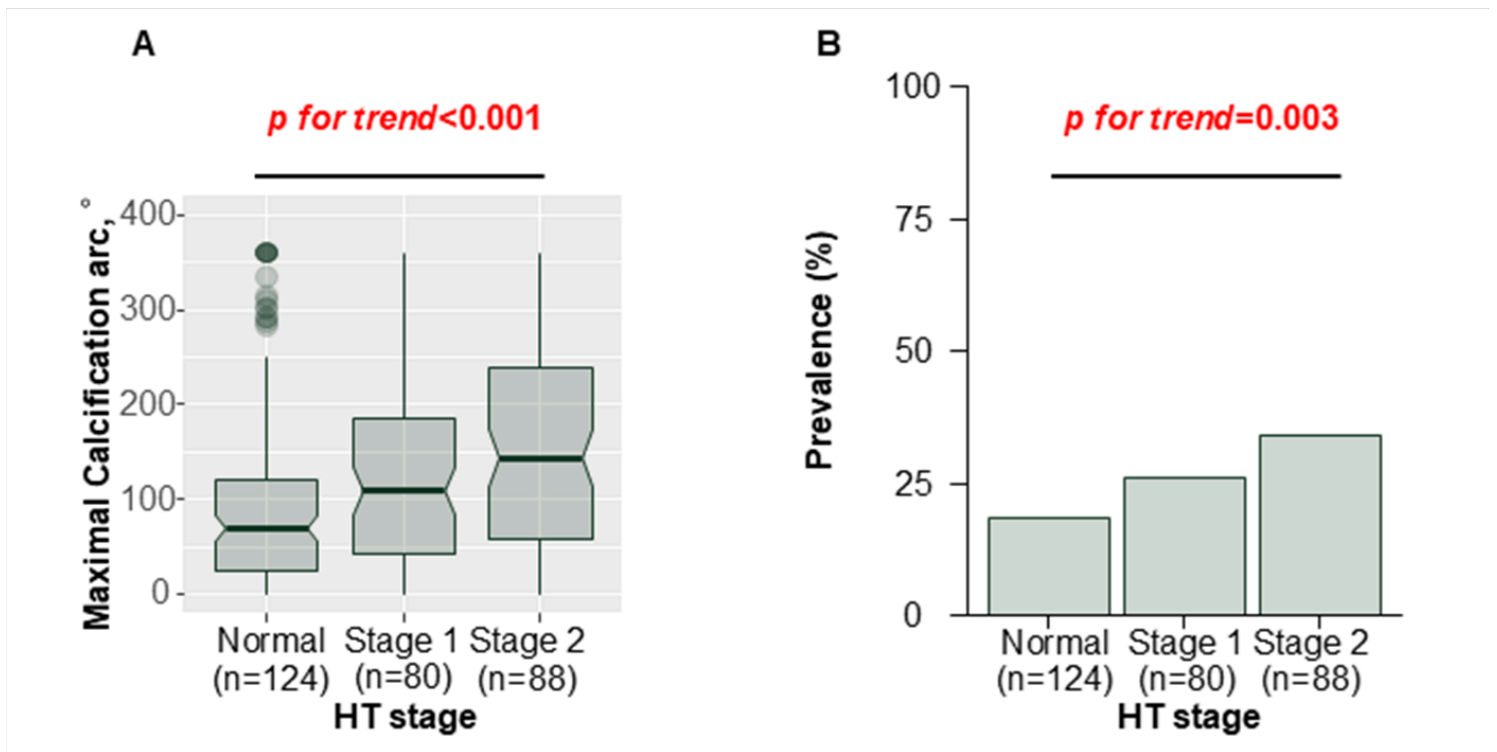


Figure 1

### The association between hypertension stages and plaque morphology

Patients were divided into three groups according to hypertension stages (normotensive, stage 1, and stage 2). (A) maximal calcification arc cross hypertension stages. (B) prevalence of lesions with a calcium score  $\geq 3$  across hypertension stages. The  $p$  values for the trend were calculated using the Jonckheere–Terpstra test for continuous variables or the Cochran–Armitage test for categorical variables. DBP, diastolic blood pressure; SBP, systolic blood pressure.

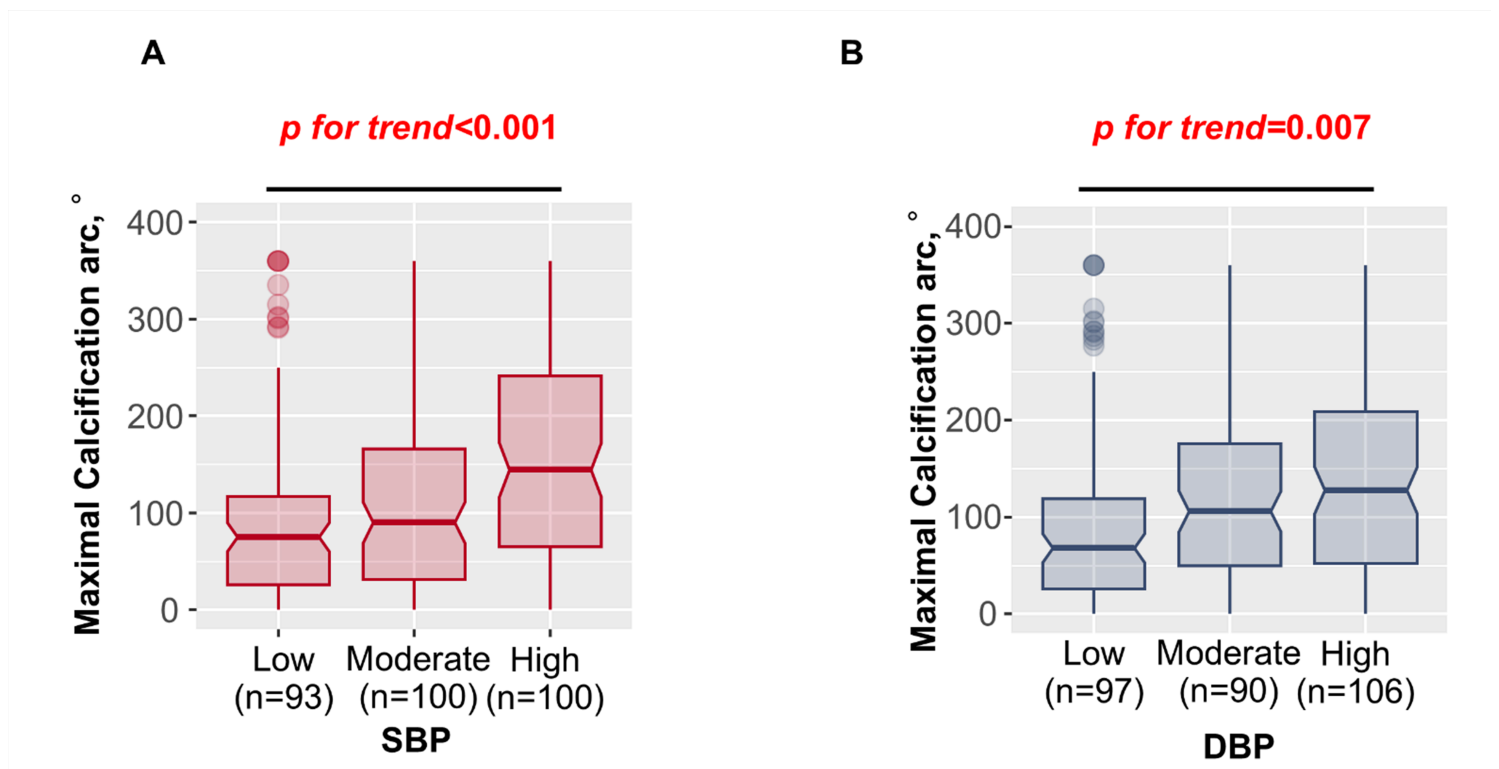


**Figure 2**

**The association of Systolic blood pressure (SBP) or Diastolic blood pressure (DBP) with calcium index.**

Patients were divided into three groups according to tertiles of SBP (Low: < 120 mmHg; Moderate: 120 – 135 mmHg; High > 135 mmHg) or DBP (Low: < 73 mmHg; Moderate: 73 – 83; High: > 83 mmHg). (A) Maximal calcification arc according to SBP and DBP tertiles. (B) Prevalence of lesions with a calcium score  $\geq 3$  across SBP and DBP tertiles. The *p* values for the trend were calculated using the Jonckheere–Terpstra test. DBP, diastolic blood pressure; SBP, systolic blood pressure.

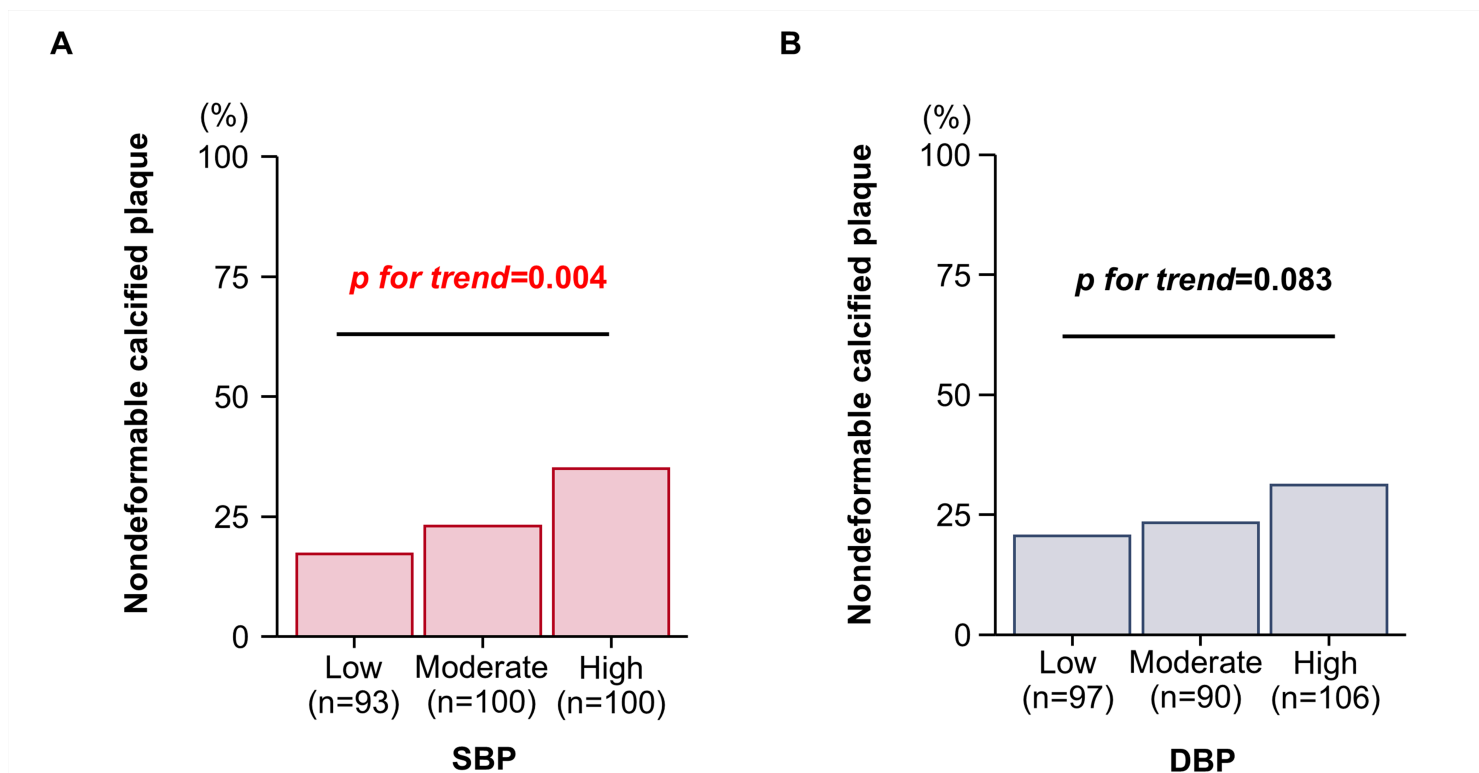


**Figure 3**

### The association of SBP or DBP with nondeformable calcified plaque.

Patients were divided into three groups according to tertiles of SBP (Low: < 120 mmHg; Moderate: 120 – 135 mmHg; High > 135 mmHg) or DBP (Low: < 73 mmHg; Moderate: 73 – 83; High: > 83 mmHg). (A) Prevalence of nondeformable calcified plaque according to SBP tertiles. (B) Prevalence of nondeformable calcified plaque according to DBP tertiles. The *p* values for the trend were calculated using the Cochran–Armitage test. DBP, diastolic blood pressure; SBP, systolic blood pressure

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalBPplaqueSR.docx](#)