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## Effects of Pitavastatin Beyond Cholesterol Reduction: Surprises and Lessons from a Prospective Randomized Open-Label Clinical Trial

Moroi M

Toho J Med 8 (1): 1–10, 2022

## 要約：

Statins (hydroxymethylglutaryl-CoA reductase inhibitors) are used globally in patients with hypercholesterolemia to prevent atherosclerotic diseases. The effectiveness of statins in reducing the number of cardiovascular events depends on the degree to which low-density lipoprotein cholesterol (LDL-C) levels are reduced. In Japan, the three most commonly used moderate-intensity statins are pitavastatin (2 mg/day), atorvastatin (10 mg/day), and rosuvastatin (2.5 mg/day). Until recently, the frequency of cardiovascular events among patients taking these statins had not been explored. We reported the outcomes of patients with hypercholesterolemia treated with either pitavastatin or atorvastatin in the TOHO lipid intervention trial using pitavastatin (TOHO-LIP). In this article, the beneficial effects of pitavastatin beyond cholesterol reduction discovered in the TOHO-LIP trial are described and a historical backdrop is provided. The subjects were patients with hypercholesterolemia with one or more risk factors for atherosclerosis, randomized to receive either pitavastatin (2 mg/day; n = 332) or atorvastatin (10 mg/day; n = 332). The follow-up period was 240 weeks. The primary composite end point was cardiovascular death, sudden death of unknown origin, nonfatal myocardial infarction, nonfatal stroke, transient ischemic attack, or heart failure requiring hospitalization. Patients who received pitavastatin treatment experienced fewer cardiovascular events during the follow-up than those who received atorvastatin treatment, although both statins produced similar effects on LDL-C levels. Subgroup analyses revealed that the cardio-ankle vascular index was significantly lower among patients in the pitavastatin group than in the atorvastatin group. Moreover, the preheparin serum lipoprotein lipase mass level, which correlates negatively with coronary atherosclerosis progression, was higher in the pitavastatin group than in the atorvastatin group. Recently, pitavastatin has been shown to have anticancer effects by inhibiting cell growth. Pitavastatin may similarly inhibit atherosclerosis-related cell growth, thereby reducing rates of cardiovascular events in high-risk patients.

**KEYWORDS:** statins, HMG-CoA reductase inhibitors, cardiovascular diseases, prevention

Association between the Clinical Incidence of Cardiac Risk and  $^{123}\text{I}$ -Betamethyl-*p*-Iodophenyl-Pentadecanoic Acid Single-Photon Emission Computed Tomography in Patients with Vasospastic Angina

Ishida S, Hashimoto H, Nakanishi R, Mizumura S, Yamazaki J, Ikeda T

Toho J Med 8 (1): 11–20, 2022

## 要約：

**Introduction:**  $^{123}\text{I}$ -Betamethyl-*p*-iodophenyl-pentadecanoic acid single-photon emission computed tomography ( $^{123}\text{I}$ -BMIPP-SPECT) is a myocardial fatty acid metabolism imaging technique that has been found to be effective in identifying high-risk patients with known ischemic heart disease. However, its efficacy in assessing vasospastic angina (VA) remains unclear. Hence, in this current study, we aimed to evaluate the association between  $^{123}\text{I}$ -BMIPP-SPECT parameters and the clinical incidence of cardiac risk in VA.

**Methods:** Among the 71 consecutive patients admitted to our hospital for ischemic heart disease who underwent  $^{123}\text{I}$ -BMIPP-SPECT, 63 (mean age:  $59 \pm 12$  years) were diagnosed with VA based on invasive coronary angiography and/or clinical examination findings.  $^{123}\text{I}$ -BMIPP-SPECT parameters, such as extent and severity scores and washout rate (WR), were calculated using  $^{123}\text{I}$ -BMIPP-SPECT data. A multivariate logistic regression model was then used to determine the correlation between  $^{123}\text{I}$ -BMIPP-SPECT parameters and major adverse cardiac events (MACEs), including

cardiac death, defined as death caused by heart failure (HF), acute myocardial infarction, lethal ventricular arrhythmias, or other definitive cardiac disorders; cardiovascular events (nonfatal acute myocardial infarction, unstable angina pectoris, and arrhythmia requiring hospitalization); and severe HF requiring hospitalization and implantable cardioverter-defibrillator treatment.

**Results:** Total 16 out of the 63 patients have reportedly experienced MACEs. Moreover, our results showed that a higher  $^{123}\text{I}$ -BMIPP WR was associated with an increased incidence of MACEs (odds ratio: 5.105, 95% confidence interval 1.503-17.344,  $p = 0.009$ ).

**Conclusions:** The findings of this current study show that  $^{123}\text{I}$ -BMIPP-SPECT WR may be associated with the clinical incidence of cardiac risk in patients with VA.

**KEYWORDS:** vasospastic angina,  $^{123}\text{I}$ -betamethyl-*p*-iodophenyl-pentadecanoic acid single-photon, emission computed tomography, major adverse cardiac event, incidence

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## In Vivo Kinematic Analysis of Bicruciate-Retaining Total Knee Arthroplasty Focused on Function of the Anterior Cruciate Ligament

Ishigaki K, Aoki H, Takamatsu R, Nishiwaki Y, Takahashi H, Nakamura T  
Toho J Med 8 (1): 21—29, 2022

### 要約 :

**Introduction:** The utility of a bi-cruciate retaining total knee arthroplasty (BCR-TKA) is uncertain. This study aims to examine whether there is a difference in the kinematics of BCR-TKA and cruciate-retaining total knee arthroplasty (CR-TKA) with a shearing force on the anterior cruciate ligament (ACL).

**Methods:** The subjects were 10 varus knees that underwent TKA (BCR: five knees, CR: five knees) at our hospital. We evaluated *in vivo* kinematics of the knee using fluoroscopy and investigated the femoral component translation relative to the tibial component from extension to maximum flexion, and the rotation angle between the components on level ground and a 10° forward slope.

**Results:** The femoral component showed gradual external rotation relative to the tibial component with flexion. In the BCR group, the rotation across the flexion angles was larger and the medial and lateral nearest points were positioned more anterior with a statistical significance under both conditions. The kinematic pathway showed a medial pivot pattern in which the lateral nearest point translated posteriorly, whereas the medial nearest point stayed until 90° flexion in the BCR group. Conversely, in 0°-20° flexion, the component rotated internally and it showed a medial pivot pattern until 20°-90° in the CR group.

**Conclusions:** There is a difference between the kinematics of BCR-TKA and CR-TKA. In the BCR group, kinematics close to screw home movement were found and these results provided evidence that conserved ACL function induced motion close to the normal knee, in comparison with CR-TKA.

**KEYWORDS:** anterior cruciate ligament, bi-cruciate retaining total knee arthroplasty, kinematics

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## Is White Blood Cell Count a Predictor of Immune-Related Adverse Events and Favorable Prognosis in the Gastric Cancer Patients Treated with Nivolumab?

Matsumoto Y, Oshima Y, Suzuki T, Yajima S, Kikuchi Y, Shimada H  
Toho J Med 8 (1): 30—38, 2022

### 要約 :

**Introduction:** Immune-related adverse events (irAEs) have been reported to be a favorable prognostic factor in patients treated with immune checkpoint inhibitors. To identify the convenient biomarkers to predict irAEs, we analyzed the relationship between pretreatment laboratory data and irAEs in gastric cancer patients treated with

nivolumab.

**Methods:** A retrospective analysis was performed on 38 patients treated with nivolumab for unresectable or recurrent gastric cancer between September 2017 and December 2019. We evaluated the relationships between pretreatment laboratory data, adverse events, and prognosis. The significance of irAE predictors was evaluated via univariate and multivariate analyses. The prognostic significance of irAE predictors was also evaluated. This study was approved by the relevant ethics committee of Toho University Omori Medical Center (No. M21048, 20108, M20300).

**Results:** In total, 14 irAEs were recorded in 13 of 38 patients (37%). The irAE (+) group showed favorable treatment response ( $P = 0.038$ ) and prognosis ( $P = 0.093$ ) in comparison with the irAE (-) group. The irAE (+) group showed low urea nitrogen, high sodium, and low white blood cell count (less than  $5100/\mu\text{l}$ ). Although low urea nitrogen and high sodium were identified to be not associated with good overall survival, the group with low white blood cell count was significantly associated with good overall survival ( $P = 0.022$ ).

**Conclusions:** A low white blood cell count at pretreatment may be a predictor of irAEs and favorable overall survival in gastric cancer patients treated with nivolumab. Gastric cancer patients with a low white blood cell count may be a good candidate for nivolumab treatment.

**KEYWORDS:** nivolumab, gastric cancer, irAE, laboratory data, white blood cell count

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## Age-Related Changes in Sound Image Localization during Lateral Gaze

Misawa T, Takeda H, Suzuki M

Toho J Med 8 (1): 39–46, 2022

### 要約 :

**Introduction:** Sound image localization is affected by eye position; however, the effect of aging on this process is unclear. This study aimed to examine the effects of age-related changes on sound image localization during lateral gaze.

**Methods:** The subjects were 34 healthy individuals (8 men and 26 women) aged 23-63 years. The binaural input sound was set to 500 Hz band noise at 50 dB, the time difference was set to 100  $\mu\text{s}$  with an audiometer, and the interaural time difference discrimination threshold was measured. A sawtooth wave was recorded when the subject changed the time difference between the left and right input sounds and moved the sound image to the center. During the measurement, the subject gazed at 0-30° to the right or 30° to the left.

**Results:** The deviation of the medial axis during gaze was significantly higher in the middle-aged and elderly group (patients aged  $\geq 40$  years) than in the young age group (patients aged  $< 40$  years), but there was no significant difference in the deviation ratio between both groups at 0° gaze. There was no significant between-group difference in the amplitude.

**Conclusions:** The medial axis is more significantly deviated in the gaze direction in the middle-aged and elderly group than in the young age group. This indicates that eye position interference has a greater effect on sound localization in middle-aged and elderly people.

**KEYWORDS:** sound image localization, eye position, gaze, age, interaural time difference

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