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Anti-Apo B-100 Autoantibody is a Marker of Unstable Coronary Plaque

Minami Imai[1], Mari Kawamura[1], Ikoi Kochi[1], Tetsuro Matsuoka[2], Shinji Kihara[1] and Hiroyasu Yamamoto[1]

[1]Department of Biomedical Informatics, Division of Health Sciences, Osaka University Graduate School of Medicine, Osaka, Japan
[2]Department of Cardiology, Hyogo Prefectural Nishinomiya Hospital, Hyogo, Japan

Aims: Cardiovascular diseases (CVD) are a global leading cause of mortality. However, few biomarkers are available to predict future coronary plaque rupture. We have recently demonstrated that low levels of anti-apolipoprotein B-100 autoantibody (anti-apo B-100 Ab) correlated with an increased CVD risk in Japanese patients with diabetes. In the present study, we examined the relationship between serum anti-apo B-100 Ab levels and coronary plaque characteristics in patients undergoing elective percutaneous coronary intervention (PCI).

Methods: We conducted iMAP®-intravascular ultrasound (IVUS) in 88 Japanese male patients undergoing elective PCI, and the five consecutive slices of IVUS images at the center of the most stenotic culprit lesion were used for identifying the plaque characteristics. The serum levels of anti-apo B-100 Ab against synthetic peptides (p45 or p210) were measured using a homemade enzyme-linked immunosorbent assay.

Results: Serum IgG levels of anti-apo B-100 Ab against both native p45 and p210 ($IgG_{N\text{-}p45}$ and $IgG_{N\text{-}p210}$) and malondialdehyde (MDA)-modified p45 and p210 ($IgG_{MDA\text{-}p45}$ or $IgG_{MDA\text{-}p210}$) showed a negative correlation with plaque burden in total male patients undergoing elective PCI. Additionally, both $IgG_{N\text{-}p45}$ and $IgG_{N\text{-}p210}$, but neither $IgG_{MDA\text{-}p45}$ nor $IgG_{MDA\text{-}p210}$, correlated negatively with necrotic and positively with fibrotic components of iMAP®-IVUS plaque characteristics in the patients with <1 month statin treatment before elective PCI ("statin-untreated" group). There was no significant correlation between anti-apo B-100 Ab and any plaque characteristics in the patients with statin treatment for 1 month or more before elective PCI ("statin-treated" group).

Conclusion: Measuring serum levels of anti-apo B-100 Ab might be helpful in the evaluation of unstable coronary plaque in male CVD patients without statin treatment.

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Key words: Antibody, Apo B-100, Cardiovascular disease, Plaque, Vulnerability

Abbreviations: Ab, antibody; Apo, apolipoprotein; CRP, C-reactive protein; CVD, cardiovascular diseases; IL, interleukin; IVUS, intravascular ultrasound; LDL, low-density lipoprotein; MDA, malondialdehyde; SMC, smooth muscle cell; VLDL, very low-density lipoprotein

Introduction

In the past two decades, cardiovascular diseases (CVD) and other noncommunicable diseases have been entrenched as the major causes of preventable health loss from disease in every region worldwide[1]. According to the Global Burden of Disease 2016 Study, CVD alone accounted for 20% of total burden in women and 24% of total burden in men[2], and the leading cause of total global CVD burden was ischemic heart disease, followed by stroke[3]. It is well known that the risk factors for CVD include high blood pressure, hypercholesterolemia, diabetes mellitus, obesity, and tobacco usage and that improving these lifestyle factors would be crucial in preventing and reducing the incidence of acute coronary events[4]. However, the onset of acute coronary events is often preceded by the awareness of

Address for correspondence: Department of Biomedical Informatics, Division of Health Sciences, Osaka University Graduate School of Medicine, 1-7 Yamadaoka, Suita City, 565-0871, Osaka, Japan E-mail: yamamoto@sahs.med.osaka-u.ac.jp

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such CVD risk factors.

Acute coronary events are associated with two atherosclerotic plaque morphologies, namely, plaque rupture and plaque erosion[5], and the former has been detected at the culprit lesion site in 59%–75% of patients[6, 7]. Therefore, intensive research has been conducted to identify coronary atherosclerotic plaques that are prone to rupture, i.e., "vulnerable plaques." Among such vulnerable plaques, the thin-cap fibroatheroma characterized by a large necrotic core covered by a thin layer of the fibrous cap has been considered to be at the greatest risk of rupture[8, 9]. Intravascular ultrasound (IVUS) has been applied for *in vivo* intracoronary imaging[10], and the real-time quantification of coronary plaques using iMAP®-IVUS (Boston Scientific, Boston, MA) can categorize them into four different plaque characteristics (i.e., fibrotic, necrotic, lipidic, and calcified), thus helping to presume their vulnerability levels[11].

Elevated low-density lipoprotein (LDL) cholesterol is one of the most established CVD risk factors. The evidence generated from genetic, observational, and randomized studies has consistently demonstrated a causal, log-linear association between exposure to LDL and CVD risk[12]. Lipid-lowering therapies, especially statin treatment to specifically reduce LDL levels, have been shown to reduce the risk of cardiovascular events by 20% for each decreased LDL cholesterol level of 1 mmol/L (40 mg/dL), even in people considered as at low cardiovascular risk[13]. Apolipoprotein B (apo B) is a large protein enveloping the surface of LDL as a macromolecular scaffold to provide structural integrity, and the majority of apo B-containing lipoproteins (up to approximately 70 nm in diameter) can promote plaque formation, except for fully formed chylomicrons and large very low-density lipoproteins (VLDLs)[14]. Furthermore, it was demonstrated that the retention of apo B-containing lipoproteins within the artery wall induces a self-accelerating process by promoting their proinflammatory modifications, evoking inflammatory cellular responses, and entrapping further lipoproteins, which leads to the development of atherogenic lesions[15-17]. Therefore, blocking the retention of apo B-containing lipoproteins should be a potential therapeutic target.

In this context, several studies have explored the relationship between anti-apo B-100 autoantibody (anti-apo B-100 Ab) and atherosclerosis[18-20]. We have also recently reported that serum levels of anti-apo B-100 Ab were significantly lower in patients with diabetes with macroangiopathy than in those without macroangiopathy[21]. In the present study, we further investigated the clinical significance of anti-apo B-100 Ab in male patients undergoing elective percutaneous coronary intervention (PCI) and found that serum levels of anti-apo B-100 Ab showed a negative correlation with both coronary plaque burden and plaque instability marker, necrotic component, in the patients with less than 1 month statin treatment before the elective PCI. Therefore, we suggest that anti-apo B-100 Ab could be a novel marker for determining plaque stability/vulnerability.

Methods

Patients

Study participants were enrolled at the Department of Cardiology in Hyogo Prefectural Nishinomiya Hospital, Japan. In this single-center study, data were reviewed for 88 consecutive male patients who underwent elective PCI and IVUS, using iMAP®-IVUS. We excluded those who were older than 82 years, had renal dysfunction (serum creatinine >1.5 mg/dL) or malignant disease, or whose target lesions were chronic total occlusion or in-stent restenosis. The patients were divided into two groups according to the duration of statin treatment before the elective PCI: the patients with less than 1 month statin treatment ("statin-untreated" group) and those with statin treatment for 1 month or more before the elective PCI ("statin-treated" group). The ethics committees of both Hyogo Prefectural Nishinomiya Hospital and Osaka University Graduate School of Medicine approved the present study. Each patient provided written informed consent.

iMAP®-IVUS

IVUS was conducted using a 40 MHz catheter (Atlantis™ SR Pro2 or OptiCross™ Imaging Catheter, Boston Scientific, Marlborough, MA) and analyzed, as described previously[22]. We conducted a volumetric analysis of the five consecutive slices of IVUS images at the center of the most stenotic culprit lesion and calculated the plaque burden and percentage contribution of each component to the entire plaque.

Measurement of Serum Parameters and Antibody Levels Against Anti-Apolipoprotein B-100

Fasting serum biochemical markers were measured in commercial laboratories. The serum levels of anti-apo B-100 Ab against two native or malondialdehyde (MDA)-modified synthetic peptides (p45 and p210) were measured using homemade enzyme-linked immunosorbent assay (ELISA), as previously reported[21].

Statistical Analysis

Statistical analysis was conducted using JMP Pro

Table 1. Characteristics of the patients

1) Clinical parameters

	mean ± SD	range
Age (year)	68 ± 10	(37-82)
Body Mass Index (kg/m^2)	24.7 ± 3.5	(16.0-34.5)
TC (mg/dL)	169 ± 36	(106-310)
TG (mg/dL)	144 ± 85	(50-434)
LDL-C (mg/dL)	99 ± 29	(46-210)
HDL-C (mg/dL)	42 ± 9	(23-80)
RLP-C (mg/dL)	8.0 ± 5.5	(1.6-47.7)
Fasting plasma glucose (mg/dL)	111 ± 35	(77-245)
HbA1c (%)	6.4 ± 1.2	(4.9-10.2)
Creatinine (mg/dL)	0.90 ± 0.21	(0.48-1.62)
hsCRP (mg/dL)	0.33 ± 0.66	(0.01-4.34)
$IgG_{N\text{-}p45}$	0.519 ± 0.434	
$IgG_{N\text{-}p210}$	0.587 ± 0.424	
$IgG_{MDA\text{-}p45}$	0.546 ± 0.340	
$IgG_{MDA\text{-}p210}$	0.557 ± 0.348	

TC; total cholesterol, TG; triglyceride, RLP-C; remnant-like particles-cholesterol, hsCRP; high sensitive CRP

2) Complications

	(+) / (-)	positive rate
Diabetes	36 / 52	40.9%
Hypertension	60 / 28	68.2%
Dyslipidemia	50 / 38	56.8%
Smoking (ex- or current)	60 / 28	68.2%

version 14.0.0 (SAS Institute Inc., Cary, NC). Data are presented as mean ± standard deviation (SD) values. Spearman's correlation coefficient and multiple regression analysis were used to evaluate the association between two variables. *P* values of <0.05 showed statistical significance.

Results

Patients

Table 1 details the demographic and clinical characteristics of the enrolled 88 male patients of elective PCI. The average age and body mass index were 68 ± 10 years and 24.7 ± 3.5 kg/m^2, respectively. The rates of patients in diabetes, hypertension, and dyslipidemia were 40.9%, 68.2%, and 56.8%, respectively. The rate of ex-smokers or current smokers was 68.2%. Because of the medical treatment including statins, serum LDL-C levels were well controlled (99 ± 29 mg/dL). Serum glucose levels were also well controlled, and the mean HbA1c level was 6.4% ± 1.2%. The results of the homemade ELISA revealed that the serum levels of anti-apo B-100 Ab of IgG class against p45 ($IgG_{N\text{-}p45}$) and p210 ($IgG_{N\text{-}p210}$) were 0.519 ± 0.434 and 0.587 ± 0.424, respectively. Serum IgG levels against MDA-modified p45 ($IgG_{MDA\text{-}p45}$) and p210 ($IgG_{MDA\text{-}p210}$) were 0.546 ± 0.340 and 0.557 ± 0.348, respectively. The number of patients in the statin-treated and statin-untreated groups was 43 and 45, respectively, and there were no significant differences in any serum anti-apo B-100 Ab levels between these two groups **(Supplemental Fig. 1)**.

Characteristics of Coronary Plaque Evaluated using iMAP®-IVUS

The characteristics of the target coronary plaque were evaluated using the five consecutive slices of iMAP®-IVUS images at the center of the most stenotic culprit lesion. The average plaque burden and total plaque volume were 71.3% ± 7.7% and 24.2 ± 8.0 mm^3, respectively **(Table 2)**. The percentage of each component within the target plaque was as follows: necrotic, 32.8% ± 12.3%; lipidic, 11.7% ± 3.2%; fibrotic, 53.0% ± 14.2%; and calcified, 3.0% ± 2.5%.

Relationship between Serum Anti-Apo B-100 Ab Levels and Plaque Characteristics

First, we analyzed the correlation between serum

Table 2. Characteristics of the target coronary plaque

	mean ± SD	range
Plaque burden (%)	71.3 ± 7.7	(52.5-84.4)
Total plaque volume (mm^3)	24.2 ± 8.0	(46.0-8.5)
Necrotic components (%)	32.8 ± 12.3	(9.6-63.0)
Lipidic components (%)	11.7 ± 3.2	(5.2-20.6)
Fibrotic components (%)	53.0 ± 14.2	(21.4-84.9)
Calcified components (%)	3.0 ± 2.5	(0.2-15.0)
Necrotic plus Lipidic components (%)	44.5 ± 13.7	(14.8-76.5)
Fibrotic plus Calcified components (%)	56.0 ± 13.7	(24.0-85.6)

Table 3. Correlation between plaque characteristics and anti-apo B-100 antibodies

	$IgG_{N\text{-}p45}$		$IgG_{N\text{-}p210}$		$IgG_{MDA\text{-}p45}$		$IgG_{MDA\text{-}p210}$	
	ρ	p	ρ	p	ρ	p	ρ	p
Plaque burden	−0.271	0.011	−0.302	0.004	−0.290	0.006	−0.230	0.031
Total plaque volume	−0.171	0.111	−0.205	0.055	−0.060	0.581	−0.141	0.191
Necrotic components	−0.156	0.147	−0.140	0.195	−0.149	0.167	−0.126	0.242
Lipidic components	−0.029	0.792	−0.076	0.482	0.046	0.674	−0.007	0.947
Fibrotic components	0.138	0.200	0.128	0.236	0.130	0.228	0.131	0.225
Calcified components	0.039	0.720	0.046	0.671	−0.093	0.387	−0.065	0.548
Necrotic plus Lipidic components	−0.130	0.228	−0.127	0.240	−0.117	0.279	−0.107	0.319
Fibrotic plus Calcified components	0.128	0.236	0.124	0.250	0.113	0.293	0.103	0.340

anti-apo B-100 Ab levels and plaque characteristics in the total enrolled patients. We found that the plaque burden negatively correlated with autoantibody against both native and MDA-modified p45 and p210 significantly ($IgG_{N\text{-}p45}$: $\rho = -0.271$, $p = 0.011$; $IgG_{N\text{-}p210}$: $\rho = -0.302$, $p = 0.004$; $IgG_{MDA\text{-}p45}$: $\rho = -0.290$, $p = 0.006$; $IgG_{N\text{-}p210}$: $\rho = -0.230$, $p = 0.031$) **(Table 3)**. None of the abovementioned four plaque components of the target lesion showed correlation with any serum levels of anti-apo B-100 Ab, but total plaque volume had a negative correlation trend with the serum $IgG_{N\text{-}p210}$ levels ($\rho = -0.205$, $p = 0.055$).

Statin treatment has been widely used for patients with coronary artery diseases, to achieve both lipid-lowering effects and stabilization of the plaques. Then, we conducted a sub-analysis, according to the duration of statin treatment before the elective PCI. In the patients of the statin-untreated group, the plaque burden showed a negative correlation with both $IgG_{N\text{-}p45}$ ($\rho = -0.355$, $p = 0.017$) and $IgG_{N\text{-}p210}$ levels ($\rho = -0.356$, $p = 0.049$) significantly and a negative correlation trend with $IgG_{MDA\text{-}p210}$ levels ($\rho = -0.263$, $p = 0.081$) **(Table 4 and Fig. 1)**. Total plaque volume negatively and significantly correlated with $IgG_{N\text{-}p210}$ ($\rho = -0.330$, $p = 0.027$) and had a negative correlation trend with $IgG_{N\text{-}p45}$ ($\rho = -0.277$, $p = 0.065$). Additionally, $IgG_{N\text{-}p45}$ levels correlated negatively with necrotic components ($\rho = -0.300$, $p = 0.046$) significantly and had a negative correlation trend with necrotic plus lipidic components ($\rho = -0.268$, $p = 0.076$). They also correlated positively with the fibrotic components ($\rho = 0.328$, $p = 0.028$) significantly and had a correlation trend with the fibrotic plus calcified components ($\rho = 0.260$, $p = 0.085$). $IgG_{N\text{-}p210}$ levels showed a significant positive correlation with the fibrotic component ($\rho = 0.295$, $p = 0.049$), whereas a negative correlation trend with the necrotic component ($\rho = -0.270$, $p = 0.073$). In the statin-treated group, only $IgG_{MDA\text{-}p45}$ levels had a negative correlation trend with plaque burden ($\rho = -0.298$, $p = 0.052$).

Discussion

In the present study conducted in patients with elective PCI, we found that serum IgG levels of anti-apo B-100 Ab showed a significant correlation with the plaque characteristics of the culprit coronary arteries as follows: 1) serum IgG levels of apo B-100 Ab negatively correlated with plaque burden, and 2) they also correlated with necrotic and fibrotic components, negatively and positively, respectively. These results suggest that anti-apo B-100 Ab could be used as a predictable marker for determining future

Table 4. Correlation between plaque characteristics and apo B-100 antibodies in Statin-treated and -untreated groups

Statin-untreated group ($n=45$)

	$IgG_{N\text{-}p45}$		$IgG_{N\text{-}p210}$		$IgG_{MDA\text{-}p45}$		$IgG_{MDA\text{-}p210}$	
	ρ	p	ρ	p	ρ	p	ρ	p
Plaque burden	−0.355	0.017	−0.356	0.049	−0.237	0.117	−0.263	0.081
Total plaque volume	−0.277	0.065	−0.330	0.027	−0.041	0.791	−0.225	0.137
Necrotic components	−0.300	0.046	−0.270	0.073	−0.148	0.332	−0.169	0.266
Lipidic components	−0.144	0.345	−0.151	0.322	0.123	0.423	0.021	0.894
Fibrotic components	0.328	0.028	0.295	0.049	0.175	0.250	0.218	0.151
Calcified components	−0.130	0.394	−0.133	0.385	−0.317	0.034	−0.178	0.242
Necrotic plus Lipidic components	−0.268	0.076	−0.238	0.115	−0.075	0.624	−0.141	0.355
Fibrotic plus Calcified components	0.260	0.085	0.232	0.126	0.067	0.663	0.133	0.382

Statin-treated group ($n=43$)

	$IgG_{N\text{-}p45}$		$IgG_{N\text{-}p210}$		$IgG_{MDA\text{-}p45}$		$IgG_{MDA\text{-}p210}$	
	ρ	p	ρ	p	ρ	p	ρ	p
Plaque burden	−0.183	0.240	−0.205	0.187	−0.298	0.052	−0.213	0.171
Total plaque volume	−0.034	0.831	−0.025	0.875	−0.048	0.758	−0.081	0.608
Necrotic components	−0.042	0.788	−0.005	0.974	−0.190	0.222	−0.075	0.635
Lipidic components	0.080	0.609	−0.001	0.996	−0.041	0.793	−0.067	0.668
Fibrotic components	−0.049	0.757	−0.062	0.694	0.124	0.428	0.045	0.776
Calcified components	0.239	0.123	0.263	0.088	0.112	0.475	0.058	0.712
Necrotic plus Lipidic components	−0.034	0.830	−0.022	0.887	−0.200	0.198	−0.095	0.546
Fibrotic plus Calcified components	0.029	0.855	0.016	0.918	0.196	0.207	0.090	0.568

acute coronary events in male patients with CVD.

CVD remains a major cause of premature death and chronic disability in several countries[23]. Patients with CVD often experience acute coronary syndromes and/or sudden cardiac death when the plaque ruptures[24]. Common culprit lesions are ruptured coronary plaques with superimposed thrombus, and the precursors of such lesions are known as vulnerable plaques that depend on four features, namely, a large lipid core, a thin fibrous cap covering the lipid core, inflammation in the cap due to macrophages and T cells, and no significant stenosis in coronary angiography[25, 26]. The plaque ruptures where the fibrous cap is thinner and heavily infiltrated with macrophages, and there are probably two concurrent mechanisms responsible for the thinning of fibrous caps. One is the gradual loss of smooth muscle cells (SMCs) from the fibrous cap[27]. At the same time, macrophages degrade the collagen-rich cap matrix, and the site of infiltrating macrophages is occupied by the necrotic core. In some lesions, isolated lipid pools grow into confluent necrotic cores infiltrated by macrophages. This process irreversibly disrupts the normal structure of the intima and leaves behind a matrix-devoid gruel of lipids and cell debris[28]. Furthermore, apoptosis and secondary necrosis of foam cells and SMCs are believed to be an important cause for the development of the necrotic core[29].

The primary challenge that we face today is to identify patients at high risk of acute coronary events before they occur. Multiple devices have been introduced to evaluate plaque vulnerability, such as IVUS, virtual-histology IVUS (VH-IVUS), optical coherence tomography, coronary angioscopy, CT coronary angiography, and near-infrared spectroscopy[30]. Among these modalities, IVUS was introduced in the late 1990s and has been the standard for intravascular imaging in catheterization laboratories. IVUS imaging has an advantage of excellent tissue penetration, enabling the visualization of the entire vessel structures and further analysis of vessel remodeling. Overcoming the problems of low spatial resolution of IVUS and its gray-scale representation, the developed VH-IVUS demonstrates distinct plaque characteristics by superimposing a color scheme on gray-scale images of IVUS. VH-IVUS, iMAP®-IVUS, and integral backscatter IVUS (IB-IVUS) provide similar results when evaluating plaque composition; however "lipid pools" evaluated by IB-IVUS correlated with "necrosis" but not with

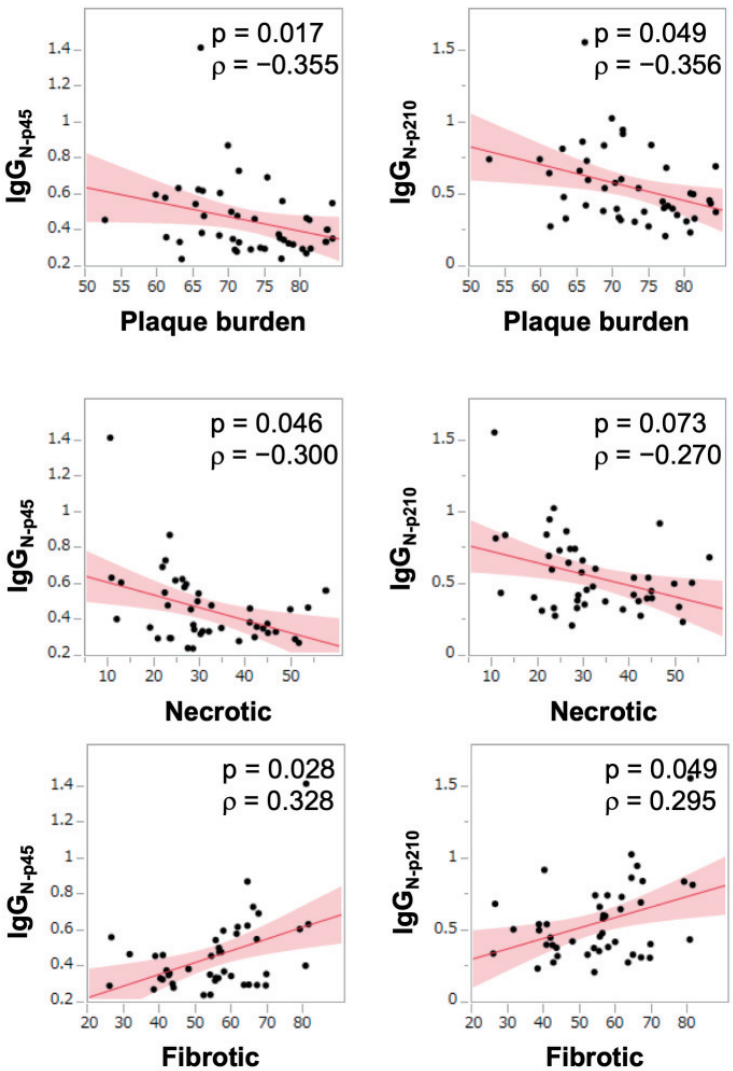

Fig. 1. Correlation between anti-apo B-100 antibodies and plaque characteristics in the statin-untreated patients

The serum IgG levels of anti-apolipoprotein B autoantibodies ($IgG_{N\text{-}p45}$ and $IgG_{N\text{-}p210}$) were compared with plaque characteristics (plaque burden and necrotic or fibrotic component) in the statin-untreated group (n=45).

the "lipid" component evaluated by iMAP®-IVUS[31, 32].

Besides these various diagnostic imaging devices, noninvasive serum biomarkers have been developed to prevent acute coronary syndrome. The major candidates have been inflammation-associated markers, because inflammation and immune cell activation are involved in the vulnerability of the plaque to rupture and thrombosis, such as C-reactive protein (CRP), cytokines (interleukin (IL)-6 and IL-18), chemokines (monocyte chemoattractant protein-1), lipid and its associated molecules (oxidized apo A-1, oxidized LDL, lipoprotein-associated phospholipase A2 (PLA2), and secretory PLA2), and matrix metalloproteinases (reviewed by Shah PK[33]); however, to date, no established marker has been identified. Serum CRP levels were found to correlate with several known risk factors and inflammation in a large cohort without known CVD[34], and another study reported that an assessment of serum CRP or fibrinogen level could help prevent one additional event over a period of 10 years for every 400 to 500 people screened who have intermediate CVD risk[35]. However, the association between CRP and plaque stability was unclear. In the present study, serum CRP levels correlated with neither plaque burden nor plaque component in both the total study participants and in the statin-untreated group **(Supplemental Table 1)**.

CVD is triggered by an elevated serum LDL-C level. Recent research indicated that not only cholesterol-rich LDL but also other apo B-containing lipoproteins, including VLDL and their remnants, intermediate-density lipoprotein, and lipoprotein(a),

are directly implicated in the development of atherosclerotic CVD[36]. In the present study, we demonstrated that serum anti-apo B-100 Ab, $IgG_{N\text{-}p45}$, and $IgG_{N\text{-}p210}$ levels correlated negatively with plaque burden and necrotic plaque component and positively with fibrotic plaque component in the statin-untreated group, suggesting that $IgG_{N\text{-}p45}$ and $IgG_{N\text{-}p210}$ are useful for predicting vulnerable plaques, at least for patients without statin treatment. These results are in line with previous reports showing the negative correlation between serum IgG levels ($IgG_{N\text{-}p45}$ and $IgG_{N\text{-}p210}$) and cardiovascular disease[19, 20, 37], cardiovascular mortality[38], coronary calcification in type 2 diabetes[39], and early atherosclerosis in healthy participants[40]. Our observation that the autoantibodies against MDA-modified apo B-100 and plaque burden were negatively correlated was also in line with the previous reports showing the reduced risk of cardiovascular death in those with high serum levels of $IgG_{MDA\text{-}p45}$ and $IgG_{MDA\text{-}p210}$ [38, 41]. The anti-atherogenic effects of autoantibodies were reported in mice immunized with apo B peptides[42-44], although the anti-atherogenic mechanisms of these autoantibodies have not been fully elucidated. Recently, some direct actions of autoantibody on monocyte and macrophage have been reported. These studies demonstrated reduced TNF-α expression in oxLDL-treated monocytes by $IgG_{MDA\text{-}p45}$ and enhanced cholesterol efflux from macrophage through increasing ABCA1 expression by anti-p210 Ab, although further investigation is needed[41, 42].

Additionally, it was reported that monoclonal antibodies against apo B-binding sites on glycosaminoglycan chains within the arterial matrix could decrease the retention of intra-arterial lipoproteins and hence could prevent the progression of atherosclerosis in apo E-deficient mice[43, 44]. Statin therapy can reduce CVD events[45] through the significant reduction of lipid-rich necrotic core volume[46], and this mechanism might have resulted in the statistically insignificant correlation between serum anti-apo B-100 Ab levels and plaque instability in the statin-treated group in the present study. Therefore, further investigation would be needed to elucidate the full range of anti-inflammatory and anti-atherogenic effects of these autoantibodies.

The present study has some limitations. This was a cross-sectional and single-center study with a relatively small sample size and limited clinical parameters to be analyzed. Further larger case-control studies are required to confirm our results.

To conclude, serum levels of anti-apo B-100 Ab, especially $IgG_{N\text{-}p45}$, and $IgG_{N\text{-}p210}$, can be used to evaluate residual CVD risk in Japanese male patients of elective PCI.

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Disclosure Summary

There are no financial conflicts of interest to disclose.

Contribution Statement

M.I., M.K., I.K., and H.Y. performed research and clinical data analysis; T.M. performed clinical work and analysis; H.Y. and S.K. designed research, and M.I., S.K., and H.Y. wrote the manuscript.

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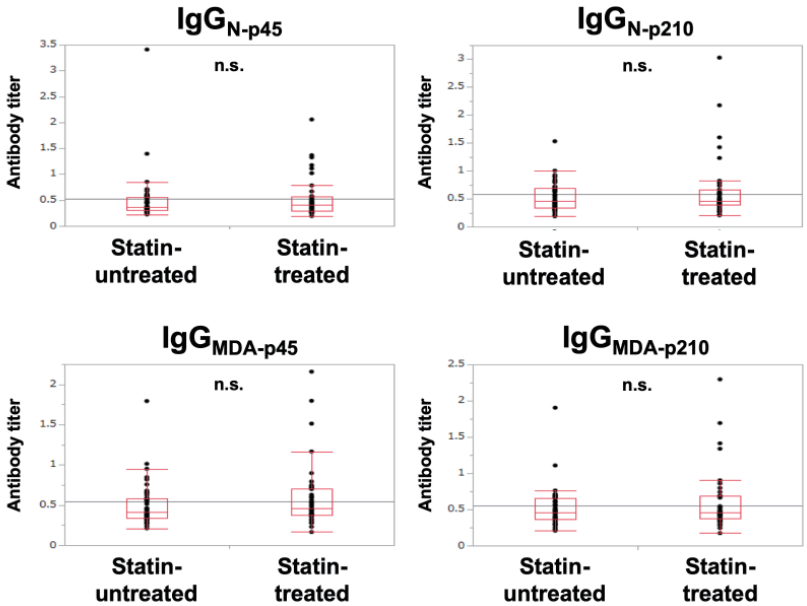

Supplemental Fig. 1. Comparison of serum levels of anti-apo B-100 antibodies in the statin-treated and -untreated group

The serum IgG levels of anti-apolipoprotein B autoantibodies ($IgG_{N\text{-}p45}$, $IgG_{N\text{-}p210}$, $IgG_{MDA\text{-}p45}$, and $IgG_{MDA\text{-}p210}$) were compared in statin-treated ($n=43$) and statin-untreated groups ($n=45$).

Supplemental Table 1. Correlation between serum hsCRP levels and plaque characteristics

	hsCRP	
	ρ	p
Plaque burden	0.047	0.669
Total plaque volume	0.080	0.460
Necrotic components	-0.014	0.896
Lipidic components	0.053	0.629
Fibrotic components	0.036	0.738
Calcified components	-0.126	0.244
Necrotic plus Lipidic components	-0.006	0.957
Fibrotic plus Calcified components	0.005	0.960