Serum uric acid and the vulnerability of carotid atherosclerotic plaque measured by Magnetic Resonance Imaging Division of Internal Medicine, Chiba prefectural Togane Hospital¹⁾, Division of Radiology, Chiba Cardiovascular Center²⁾ Hiroki Kagaya¹, Hirohumi Watanabe², Yuichiro Yoshikawa¹, Takahiro Kageyama², Shigeki Imamura¹, Aizan Hirai¹

Carotid-wall intima-media thickness (IMT) is a surrogate marker of atherosclerosis associated with cardiovascular risk factors and with cardiovascular outcomes. MR imaging of carotid plaque has been shown to be superior to the diagnostic assessment of plaque vulnerability at high risk of rupture, and to provide information useful to the choice of treatment. Regression of plaque has been reported by intensive statin therapy (IST). The effect of IST on the characteristics of carotid plaques, especially on the instability of plaques was determined using a combination of ultrasonography and MR imaging. In the present investigation, 572 patients having max IMT over 1.5mm were included. Among them, 445 patients (234 males and 211 females, average age was 70 \pm 9.9 and 70 \pm 10.1, respectively) had been treated on IST for more than 1 year before the study(IST group). On the other hand, 117 patients (49 males and 68 females) had not been treated on IST before the study(non-IST group). Serum levels of LDL-C, HDL-C LDL-C/HDL-C and uric acid of IST group and non-IST group are 68 ± 15 vs 133 ± 29 , $52 \pm 13 \text{ vs } 53 \pm 12, 1.39 \pm 0.4 \text{ vs } 2.6 \pm 0.5 \text{ and } 5.4 \pm 1.4 \text{ vs } 5.1 \pm 1.2$, respectively The black-blood method was used, and a horizontal cross-sectional image of plaque was taken with T1- and T2-weighted mode. Finally, the ratio of the lesion and the submandibular gland was determined. Plaques having the ratio of T1 evaluation more than 1.25 were defined as intraplaque hemorrhage (IPH), while those below 1.25 were defined as stable. Plaques having the ratio of T2 evaluation more than 1.25 were defined as lipid core (LC), while those below 1.25 were defined as stable. In IST group, 58% of the patients have stable plaque, 6% have IPH, 24% have LC and 11% have IPH+LC. On the other hand, 50% of the patients of non-IST group have stable plaque, 4% have IPH 33% have LC and 12% have IPH+LC. In IST group, among various parameters, only serum uric acid has strong and significant correlation with the presence of LC in carotid plaque in male (p=0.0010). Odds ratio of uric acid in the presence of LC in carotid plaque is 1.530. No such correlation was observed in female patients. Thus the present investigation provides a new insight into the role of uric acid in the vulnerability of carotid atherosclerotic plaque.

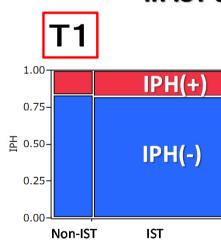
Results

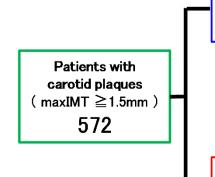
Patients Characteristics

	Non-IST group $(LDL-C \ge 100 \text{ mg/dl})$	IST group (LDL−C < 100 mg/dl)
Patients (n)	117	445
Age (year)	67.2 ± 10.3	71.2±9.9 ***
Females (%)	58.12 %	47.47 %
LDL-cholesterol (mg/dl)	133.3±29.9	68.2±15.0***
Max IMT (mm)	1.94 ± 0.66	2.12 ± 0.66 **

: P<0.01, *: P<0.0001

Carotid-wall intima-media thickness (IMT) is a surrogate marker of atherosclerosis associated with cardiovascular risk factors and with cardiovascular outcomes. MR imaging of carotid plaque has been shown to be superior to the diagnostic assessment of plaque vulnerability at high risk of rupture, and to provide information useful to the choice of treatment. Regression of plaque has been reported by intensive statin therapy (IST). The effect of IST on the characteristics of carotid plaques, especially on the instability of plaques was determined using a combination of ultrasonography and MR imaging.





LDL-C 133.3 ± 29.9

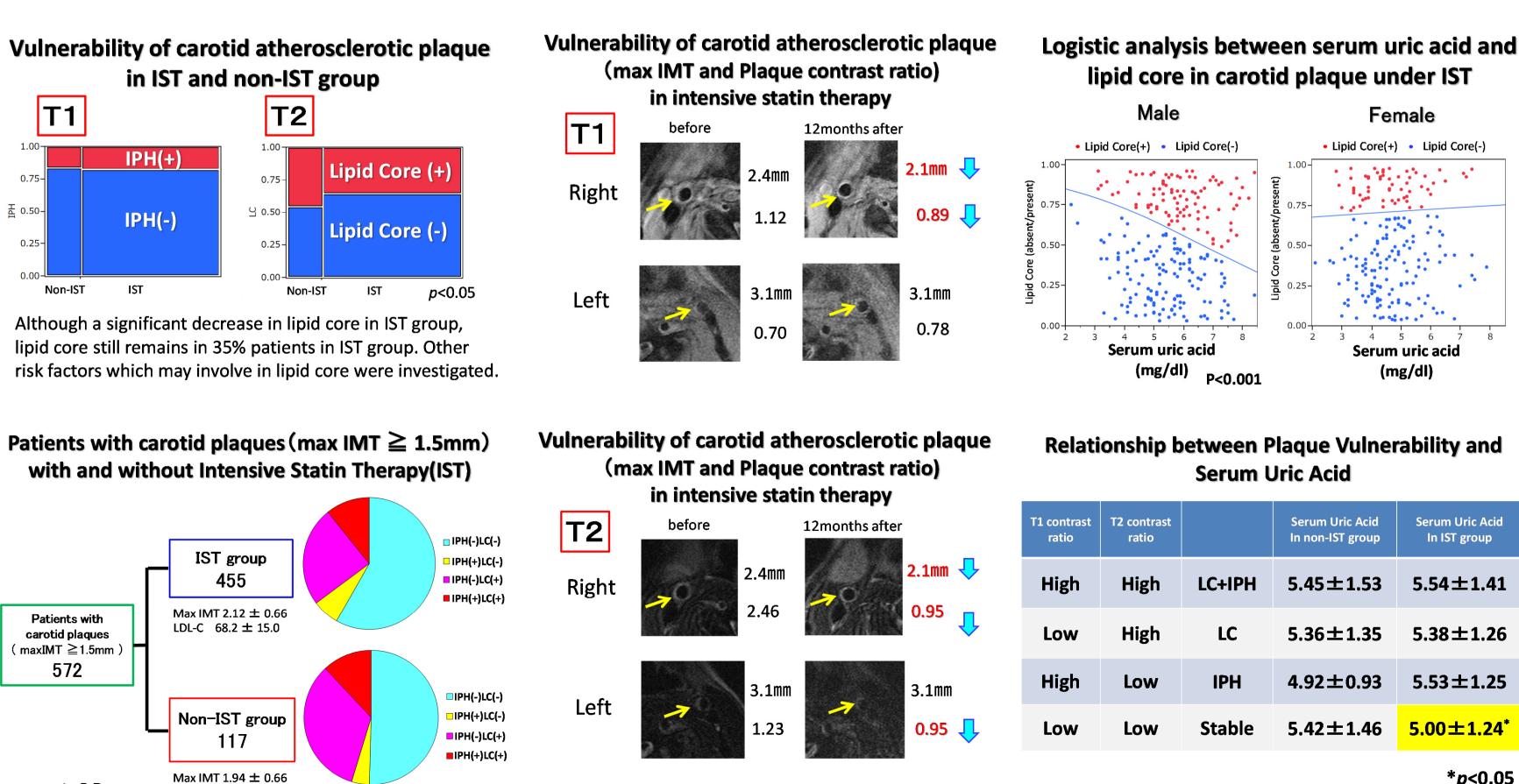
Introduction

. Subjects:

In the present investigation, 572 patients having max IMT over 1.5mm were included. Among them, 445 patients (234 males and 211 females, average age was 70 ± 9.9 and 70 ± 10.1 , respectively) had been treated on IST for more than 1 year before the study(IST group). On the other hand, 117 patients (49 males and 68 females) had not been treated on IST before the study(non-IST group). 2. Study design

The black-blood method was used, and a horizontal cross-sectional image of plaque was taken with T1- and T2-weighted mode. Finally, the ratio of the lesion and the submandibular gland was determined... 3. Statistical analysis

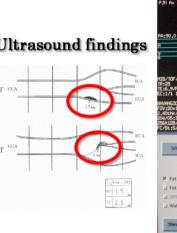
Statistical analysis was performed using the JMP® 9 software (SAS Institute Inc., Cary, NC, USA). All values are expressed as the means \pm SEM. Values of p < 0.05 were considered to indicate statistically significant differences.

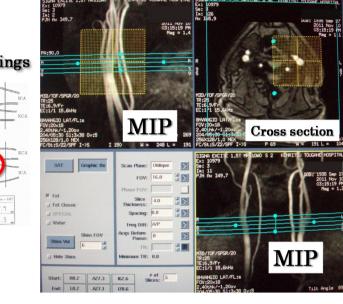


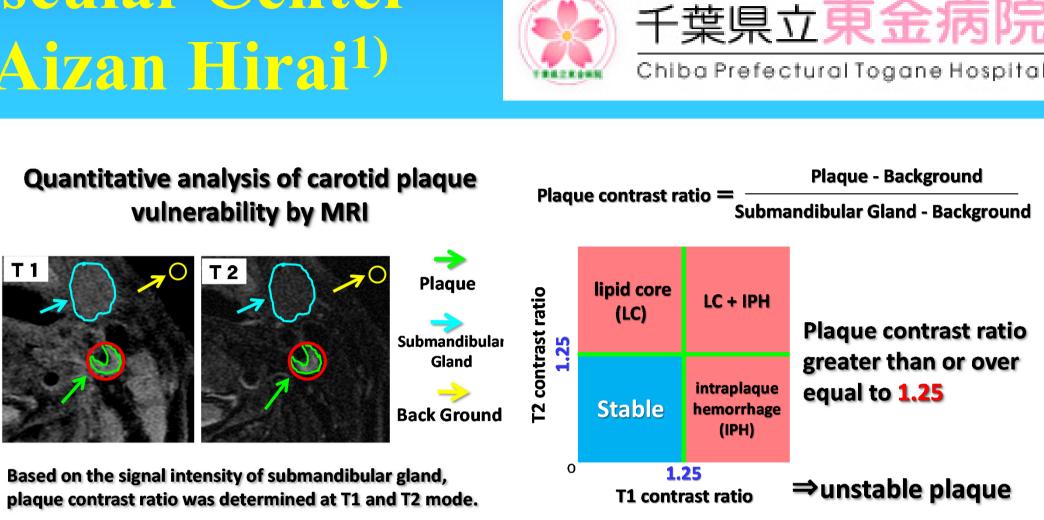
Materials and Methods

	Serum Uric Acid In non-IST group	Serum Uric Acid In IST group
C+IPH	5.45±1.53	5.54 ± 1.41
LC	5.36±1.35	5.38±1.26
IPH	4.92±0.93	5.53±1.25
table	5.42 ± 1.46	$5.00 \pm 1.24^{*}$
		*20.05

Planning for the analysis of carotid plaques by MRI







Plaques having the ratio of T1 evaluation more than 1.25 were defined as intraplaque hemorrhage (IPH), while those below 1.25 were defined as stable. Plaques having the ratio of T2 evaluation more than 1.25 were defined as lipid core (LC), while those below 1.25 were defined as stable.¹⁾

In IST group, 58% of the patients have stable plaque, 6% have IPH, 24% have LC and 11% have IPH+LC. On the other hand, 50% of the patients of non-IST group have stable plaque, 4% have IPH, 33% have LC and 12% have IPH+LC.

In IST group, among various parameters, only serum uric acid has strong and significant correlation with the presence of LC in carotid plaque in male (p=0.0010). Odds ratio of uric acid in the presence of LC in carotid plaque is 1.530. No such correlation was observed in female patients.

Discussion

The relationship between serum uric acid and carotid atherosclerotic is still debated. J.S. Bae et al suggested no association between serum uric acid and carotid IMT was found in Korean Multi-Rural Communities Cohort study²⁾. On the other hand, Y. Tavil et al described that in patients who had both hypertention and hyperuricemia had increased carotid IMT compared to the patients who did not have hyperuricemia³). The present investigation provides a new insight into the role of uric acid in the vulnerability of carotid atherosclerotic plaque.

Conclusion

- . In IST group, among various parameters, only serum uric acid has strong and significant correlation with the presence of LC in carotid plaque in male (p=0.0010). Odds ratio of uric acid in the presence of LC in carotid plaque is 1.530. No such correlation was observed in female patients.
- 2. Thus the present investigation provides a new insight into the role of uric acid in the vulnerability of carotid atherosclerotic plaque.

Acknowlegments

We would like to thank Y. Ui, H. Maeda and H. Nishihara for their excellent medical care support.

References

- 1) Watanabe Y, Nagayama M, Suga T et al. J Magn Reson Imaging 28:478-485, 2008.
- 2) J.S. Bae et al.: Atherosclerosis 231:145-151, 2013.
- 3) Y. Tavil et al.: Atherosclerosis 197:159-163, 2008.