Changes in carotid intima-media thickening in patients with type 2 diabetes mellitus: Subanalysis of the Sitagliptin Preventive Study of Intima-Media Thickness Evaluation

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LETTER TO THE EDITOR

Changes in carotid intima-media thickening in patients with type 2 diabetes mellitus: Subanalysis of the Sitagliptin Preventive Study of Intima-Media Thickness Evaluation

Type 2 diabetes mellitus is a risk factor for cardiovascular disease. Both the absolute value and progression of carotid artery intima-media thickness (IMT) are considered a marker of progression of atherosclerosis. We reported recently that treatment with sitagliptin, a dipeptidyl peptidase-4 inhibitor, attenuated the progression of carotid IMT in insulin-treated patients with type 2 diabetes mellitus compared with conventional therapy[1]. Here, we compared the efficacy of treatment with sitagliptin with that of other modalities on the progression of carotid IMT in prespecified subgroups of the Sitagliptin Preventive Study of Intima-Media Thickness Evaluation (SPIKE) registered on the University Hospital Medical Information Network Clinical Trials Registry (UMIN000007396)[1,2]. The aim of the comparison was to identify the characteristics of patients who benefited most from the sitagliptin treatment in terms of decrease in IMT.

The recruits in the original study included 282 insulin-treated Japanese type 2 diabetes mellitus patients free of past history of apparent cardiovascular disease. They were randomly allocated to either the sitagliptin group (n = 142) or the conventional treatment group (using drugs other than sitagliptin; n = 140). After the exclusion of eight patients, data of 137 patients of the sitagliptin group and 137 of the conventional treatment group were subjected to analysis. The mean-IMT of the common carotid arteries (mean-IMT-CCA) and right and left max-IMT-CCA were measured by expert sonographers at the start of the study, and the procedure was repeated after 52 and 104 weeks, as reported previously[1,2]. Figure 1 shows differences in treatment-induced delta change in carotid IMT, relative to baseline in 243 patients whose IMT data were available at baseline and 104 weeks, according to various predefined risk factors for atherosclerosis. The results showed consistent reductions in mean IMT-CCA and left max IMT-CCA, but not right max IMT-CCA, in the sitagliptin group (Figure 1). In particular, a greater reduction in carotid IMT was noted after treatment with sitagliptin in patients with risk factors for cardiovascular disease, such as higher glycated hemoglobin, higher body mass index, longer duration of type 2 diabetes mellitus, use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blocker, use of statins, worse hypertension and/or hyperlipidemia at baseline, compared with conventional treatment. These data suggest that treatment with dipeptidyl peptidase-4 inhibitors seems to prevent the progression of carotid atherosclerosis regardless of disease burden. Previous studies showed that treatment with statins and angiotensin-converting enzyme inhibitors reduces the progression of carotid atherosclerosis in patients with type 2 diabetes mellitus[3,4]. In this subgroup analysis, sitagliptin still attenuated the progression of carotid IMT, even in patients who were receiving those therapies. Thus, dipeptidyl peptidase-4 inhibitors seem to have unique and/or additive anti-atherosclerotic effects as add-on therapy to statins and/or angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers.

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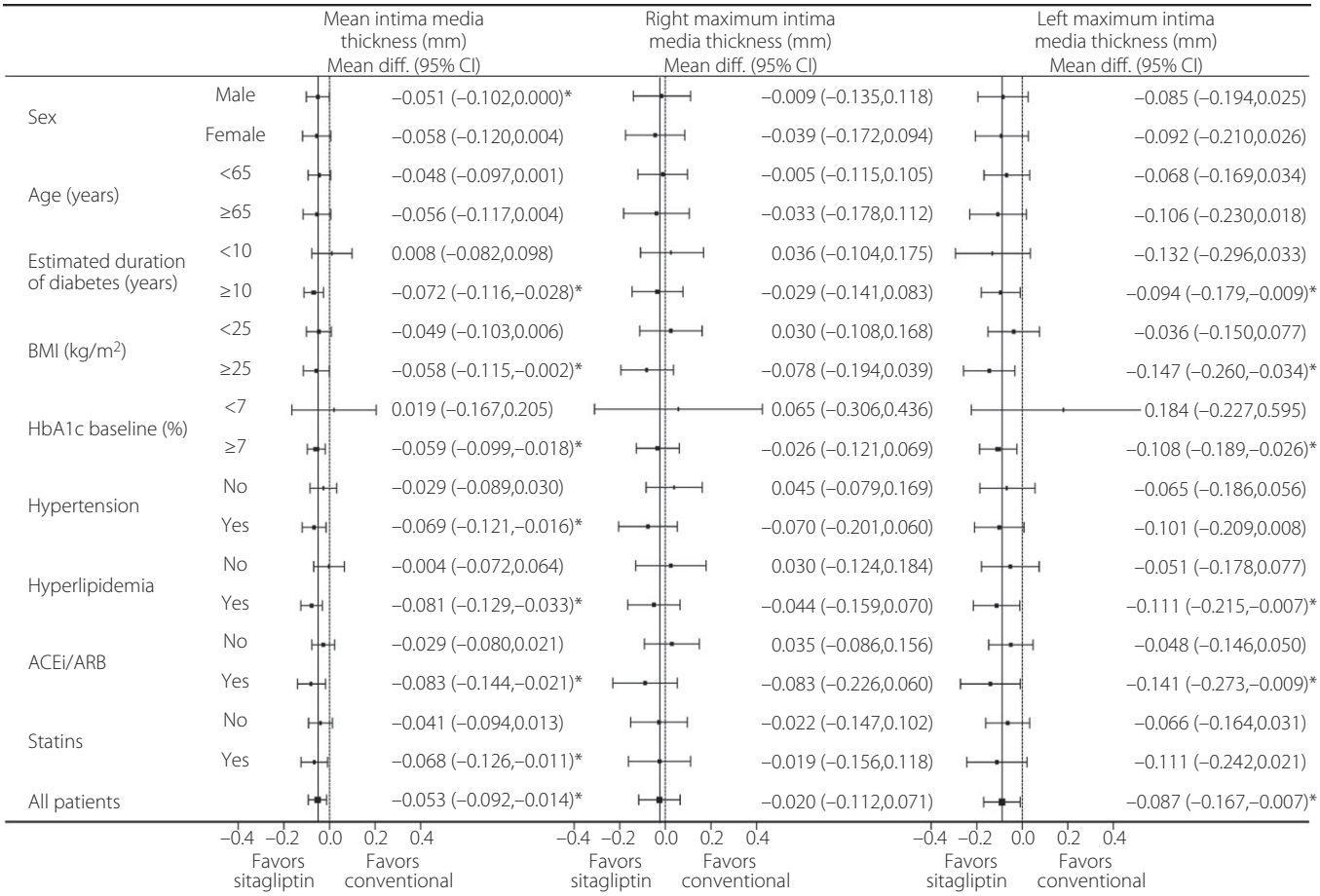

Figure 1 | Effects of sitagliptin on progression of atherosclerosis. Data are mean (95% confidence interval [CI]). Follow-up group comparisons were assessed with the Student's *t*-test. The prespecified subgroups for analysis included sex (men, *n* = 144; women, *n* = 99), age (<65 years, *n* = 116; ≥65 years, *n* = 127), body mass index (<25 kg/m^2, *n* = 132; ≥25 kg/m^2, *n* = 111), glycated hemoglobin (<7%, *n* = 16; ≥7%, *n* = 227), use of angiotensin-converting enzyme inhibitors (ACEi)/angiotensin II receptor blocker (ARB); (yes, *n* = 128; no, *n* = 115), use of statins (yes, *n* = 128; no *n* = 115), presence (*n* = 146)/absence (*n* = 97) of hypertension and presence (*n* = 154)/absence (*n* = 89) of hyperlipidemia at baseline. Solid line indicates overall treatment effect point, and broken lines indicate no effect point. **P* < 0.05 vs the conventional treatment group. There were no significant interactions between treatment group and each category.

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