

# (論文に対するコメント)

## Statins Associated With Significant Increase in Diabetes Risk

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January 9, 2012 (Boston, Massachusetts) — Statin use in postmenopausal women is associated with a significantly increased risk of diabetes mellitus, research shows [1]. New data from the **Women's Health Initiative** (WHI) hints that the risk of diabetes is higher than suggested by previous studies, with investigators reporting a 48% increased risk of diabetes among the women taking the lipid-lowering medications.

"With this study, what we're seeing is that the risk of diabetes is particularly high in elderly women, and this risk is much larger than was observed in another previous meta-analysis," senior investigator **Dr Yunsheng Ma** (University of Massachusetts Medical School, Boston) told *heartwire*. "For doctors treating patients, we would like them to really look at the risk-benefit analysis, especially in different age groups, such as older women."

**Annie Culver** (Mayo Clinic, Rochester, MN), a pharmacist and lead investigator of the study, published online January 9, 2012 in the *Archives of Internal Medicine*, said that "close monitoring and an individualized risk-versus-benefit assessment is really a good thing, as well as an emphasis on continued lifestyle changes." Culver added that as the population ages, and because these patients have a higher vulnerability to diabetes anyway, monitoring for diabetes in statin-treated patients becomes more important.

"I think the risk [of diabetes] is definitely there for statins," Culver told *heartwire*, "and I think physicians are probably aware of this risk. I think we now need more information and more research about precisely how this risk translates to different people and different populations."

### Previously Published Data on Statins and Diabetes Risk

Recently published data reported by *heartwire* highlighted the potential risk of diabetes with statin therapy. In June, **Dr Kausik Ray** (St George's University of London, UK) and colleagues published a meta-analysis of PROVE-IT, A to Z, TNT, IDEAL, and SEARCH--five trials testing high-dose statin therapy--and found a significant increase in risk of diabetes with higher doses of the lipid-lowering drugs. A meta-analysis published in the *Lancet* in 2010 by **Dr Naveed Sattar** (University of Glasgow, UK) also showed that statin therapy was associated with a 9% increased risk of diabetes.

In the present study, Culver, Ma, and colleagues analyzed data from the WHI, an analysis that included 153 840 postmenopausal women aged 50–79 years old. Information about statin use was obtained at enrollment and year three; the current analysis includes data up until 2005. At baseline, 7.0% of women were taking statins, with 30% of women taking **simvastatin**, 27% taking **lovastatin**, 22% taking **pravastatin**, 12.5% taking **fluvastatin**, and 8% taking **atorvastatin**. During the study period, 10 242 incident cases of diabetes were reported.

In an unadjusted risk model, statin use at baseline was associated with a 71% (95% CI 1.61–1.83) increased risk of diabetes. After adjusting for potential confounding variables, the risk of diabetes associated with statin therapy declined to 48% (95% CI 1.38–1.59). The association was observed for all types of statins.

"The association between diabetes risk and statin therapy was not observed with any one type of statin, and it seems to be a class effect," said Ma.

## Subgroup Risk

A significantly increased risk of diabetes was observed in white, Hispanic, and Asian women (an increased risk of 49%, 57%, and 78%, respectively). Among African Americans, who made up 8.3% of the population studied, there was a nonsignificant 18% increased diabetes risk associated with statin use at baseline. Statin use and diabetes risk was also observed in women across a range of body mass indices (BMIs <25.0, 25.0–29.9, and  $\geq 30.0$  kg/m<sup>2</sup>). Women with the lowest BMI (<25.0 kg/m<sup>2</sup>), appeared to be at higher risk of diabetes compared with obese women, a finding the investigators speculate is related to phenotype or hormonal differences between the women.

In an editorial [2], **Dr Kirsten Johansen** (University of California, San Francisco), Editor of the *Archives*, noted that the increased risk of diabetes in women without CVD has "important implications for the balance of risk and benefit of statins in the setting of primary prevention in which previous meta-analyses show no benefit on all-cause mortality."

Ma agreed, noting to *heartwire* that statins are used with increasing frequency, including in primary prevention, and--based on the **JUPITER** trial--in patients with normal LDL cholesterol, but elevated C-reactive protein (>2.0 mg/L). In the present study, baseline statin therapy was associated with a significant 46% and 48% increased risk of diabetes in women with CVD and without CVD, respectively.

Just 7% of women in the WHI study were taking statins in the analysis, but today that number would be significantly higher, making the potential risk of diabetes at the population level much more widespread. Ma said that physicians need to evaluate the risk of diabetes as well as the potential benefits of statin therapy in elderly female patients, and start statins after lifestyle interventions have been attempted.

1. Culver AL, Ockene IS, Balasubramanian R, et al. Statin use and risk of diabetes mellitus in postmenopausal women in the Women's Health Initiative. *Arch Intern Med* 2012; DOI: 10.1001/archinternmed.2011.625. Available at: <http://archinte.ama-assn.org/>.
2. Johansen KL. Increased diabetes mellitus risk with statin use. *Arch Intern Med* 2012; DOI: 10.1001/archinternmed.2011.625. Available at: <http://archinte.ama-assn.org/>.

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