

## The Risk of Bladder Cancer in Korean Diabetic Subjects Treated with Pioglitazone (*Diabetes Metab J* 2012;36:371-8)

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We sincerely appreciate the interest and comments regarding our study, "The Risk of Bladder Cancer in Korean Diabetic Subjects Treated with Pioglitazone" which was published in *Diabetes & Metabolism Journal* 2012;36(5):371-378. Our responses to Dr. Sheyu Li and Haoming Tian's comments follow.

First, that the prescription rate of pioglitazone in the group with bladder cancer was significantly lower than nonbladder cancer group may be due to the fact that the medical staffs, which were aware of the disputed association between pioglitazone and bladder cancer, were not involved in the prescription beforehand. In fact, since an argument about rosiglitazone negatively influencing bone metabolism [1] has been raised, the prescription of rosiglitazone declined sharply in this hospital. It may be possible that the prescription of pioglitazone by clinicians has also notably decreased due to the medical staff's concern of bladder cancer. This may be attributed to selection bias that is characteristic of retrospective studies, which is thought as a weak point of this study.

Second, this study found, through multiple logistic regression analysis, that history of other forms of cancer, in addition to smoking, is independent factors influencing the occurrence of bladder cancer. Smoking is a very important risk factor in case of bladder cancer [2], and the proportion of smokers in Korea is also very high [3]; therefore, we concluded that the possibility of other forms of cancer due to smoking must be taken into consideration, and we have investigated the proportion of patients with other cancers. If this proportion is not dif-

ferent between the two groups, the potential bias may actually be reduced by NOT using it as an independent variable, as you have mentioned. In reality, however, there was a significant difference between the two groups (11% in bladder cancer group vs. 2% in nonbladder cancer group,  $P < 0.001$ ), although the proportion itself was small. It was of our opinion that this must clearly be addressed.

Overall, your comments have pinpointed the weaknesses of this study very well. Nonetheless, our intention was to state that numerous factors influencing the occurrence of the disease play into the association between pioglitazone and bladder cancer; the association is not simply associated with use of a pharmaceutical agent, and these numerous confounding factors must, be taken into consideration. We hope a more accurate, reliable investigation studying whether pioglitazone indeed affects the occurrence of bladder cancer can be performed through this effort. Thank you for taking interest in this study and for your thoughtful comments.

### CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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