Arch Gynecol Obstet (2013) 287:167–168
DOI 10.1007/s00404-012-2467-3

LETTER TO THE EDITOR

# Methodological remarks concerning the recent meta-analysis on vascular endothelial growth factor polymorphism and endometriosis risk

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Received: 29 May 2012 / Accepted: 9 July 2012 / Published online: 18 July 2012


To the Editor,

We read with great interest the recent meta-analysis by Liang et al. [1], which evaluated the association between vascular endothelial growth factor (VEGF) gene polymorphisms and endometriosis risk. Eleven studies were included in their meta-analysis and their study found that the VEGF +936 C/T gene polymorphism is a risk factor for endometriosis, and not −460T/C, +405G/C, −2578A/C, −1154G/A. Nevertheless, close inspection of the study revealed some methodological issues that are worth mentioning and clarifying.

The major issue of this meta-analysis is the lack of subgroup analysis, which may make the results untrustworthy. For the +936 C/T; −460T/C and +405G/C polymorphisms, there were enough studies for subgroup analysis. The most obvious differences among the included studies were the ethnicity that the included patients in the original studies came from. For example, some studies in this meta-analysis were based on Asian populations, while the other studies were based on Caucasian patients. As previously described, ethnicity can strongly influence the distribution of gene polymorphisms [2]. Therefore, it is essential to perform the subgroup analysis by ethnicity in meta-analysis of Liang et al. [1]. For the VEGF +936 C/T polymorphism, Liang et al. [1] found that it was associated with an increased endometriosis risk. However, when stratifying for ethnicity, there was no significant association between VEGF gene +936 C/T polymorphism and endometriosis among Asians (TT + TC vs. CC: OR = 1.20, 95 % CI 0.92–1.55, $P = 0.18$, TC vs. CC: OR 1.18, 95 % CI 0.90–1.54, $P = 0.23$) and Caucasians (TT + TC vs. CC: OR = 1.18, 95 % CI 0.99–1.40, $P = 0.06$, TC vs. CC: OR 1.19, 95 % CI 1.00–1.42, $P = 0.05$). For the VEGF +405G/C polymorphism, Liang et al. [1] did not detect any association in any comparison model. However, when stratifying for ethnicity, a significantly decreased association was observed between VEGF +405G/C polymorphism and endometriosis among Asians (CC + GC vs. GG: OR = 0.74, 95 % CI 0.59–0.93, $P = 0.009$, GC vs. GG: OR 0.76, 95 % CI 0.60–0.97, $P = 0.03$), while a significantly increased association was found between VEGF +405G/C polymorphism and endometriosis among Caucasians (CC + GC vs. GG: OR = 1.17, 95 % CI 1.00–1.37, $P = 0.04$).

Moreover, close inspection of the data provided by the authors (Table 1 in the meta-analysis) revealed an issue that is worth mentioning. The data reported by Liang et al. for the study of Altinkaya et al. [3]. about VEGF +405G/C polymorphism do not seem to be in line with the data provided by Altinkaya et al. [3] in their original publication. The numbers reported by Liang et al. for CC, CG, GG, in cases for Altinkaya et al. [3], were 22-57-16, while the numbers for CC, CG, GG, in cases were 25-57-16 in Altinkaya et al.'s [3] original study. In conclusion, this letter points out interesting methodological aspects concerning the subgroup analysis by race; and it would be valuable if the authors could take into account this remark.

**Conflict of interest** None declared.

Shiqiao Tan and Ya Li have the same contributions to this study and should be considered as co-first authors.

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