Association Between the hsa-mir-27a Variant and Breast Cancer Risk: a Meta-analysis

Bin Wang, Ning Ma, Yajie Wang

Abstract

Introduction: Although a number of studies were published in the past several years on associations between hsa-mir-27a and cancer risk, the findings remain conflicting rather than conclusive. To derive a more precise effect on the association between SNP hsa-mir-27a rs895819 and breast cancer risk, we conducted a meta-analysis for the first time. Materials and Methods: Through retrieval from PubMed for the period up to August 2012, a total of four studies were identified with 3,287 cases and 4,298 controls for SNP hsa-mir-27a rs895819. We calculated summary odds ratio (ORs) and corresponding 95% confidence intervals (CIs) using a fixed effects model (when the heterogeneity was absent, P>0.10). Otherwise, the random-effects model was used. Results: We found that hsa-mir-27a rs895819 polymorphism also did not reveal any relationship with breast cancer susceptibility (AG versus AA: OR = 0.98; 95% CI, 0.73-1.32; GG versus AA: OR = 0.86; 95% CI, 0.72-1.03; AG/GG versus AA: OR = 0.92; 95% CI, 0.74-1.14), while significantly decreased risk was found among Europeans in AG versus AA and AG/GG versus AA models tested (AG versus AA: OR = 0.83; 95% CI, 0.72-0.97; GG versus AA: OR = 0.86; 95% CI, 0.71-1.05; AG/GG versus AA: OR = 0.84; 95% CI, 0.75-0.94). Conclusion: These findings suggest that hsa-mir-27a rs895819 polymorphism may play an important role in breast cancer development.

Keywords: Breast cancer - meta-analysis - gene polymorphism - ethnic groups
As breast cancer is one of the most common cancers in women, with a relatively high mortality rate, in recent years, several studies to address the association between hsa-mir-27a rs895819 variant and breast cancer risk were conducted, with contradictory results. Yang R’s study (Yang et al., 2010) reported that G-variant of rs895819 might impair the maturation of the oncogenic miR-27a and thus, is associated with familial breast cancer risk, while in Catucci I’s study (Zhang et al., 2012), no association was found.

Because the relatively small sample size in a single study might have low power to detect the effect of these polymorphisms on breast cancer risk, for better understanding of the association between hsa-mir-27a rs895819 variant and breast cancer risk, we conducted a meta-analysis to derive a more precise estimation of the association.

Materials and Methods

Identification and eligibility of relevant studies

We have attempted to include all the case control studies published to date on cancers with genotyping data for Hsa-miR-27a (rs895819). In order to obtain all possible articles we need, we searched the electronic literature PubMed for relevant reports (last search update Aug 2012) using the search terms “miRNA or microRNA and cancer and polymorphism”.

The inclusion criteria were: (1) evaluation of the has-miR-27a rs895819 polymorphism and cancer risk; (2) study designed as case-control; and (3) sufficient published data for calculating odds ratios (ORs) with their 95% confidence intervals (95% CIs).

Data Extraction

Two investigators (Wang B and Ma N) independently extracted data and reached consensus on all of the items. Data collected from these articles included the first author’s name, year of publication, country of origin, ethnicity, type of cancer, number of cases and controls, genotype frequencies for cases and controls, characteristics of cancer cases and controls, and racial descent.

Statistical analysis

The strength of association between the has-miR-27a rs895819 polymorphisms and breast cancer risk was assessed by crude ORs with their 95% CIs. The statistical heterogeneity among studies was checked by the chi-square-based Q-test (Higgins et al., 2002). When the heterogeneity was absent (P>0.10), the fixed-effects model was used to estimate the summarized OR (Mantel et al., 1959); otherwise, the random-effects model was used (DerSimonian et al., 1986). Subgroup analyses were processed, according to tumor type [categorized as breast cancer and other cancers (only breast cancer has more than two published studies)] and ethnicity (categorized as Asian and European descents). Publication bias of literatures was assessed using Begg’s funnel plot, and it was considered representative of statistically significant publication bias with P<0.05 (Egger et al., 1997). All statistical analyses were carried out with STATA software, version 10.0.

Results

Characteristics of studies

In total, four studies fulfilled the inclusion criteria (Yang et al., 2010; Sun et al., 2010; Zhang et al., 2012; Catucci et al. 2012) with 2763 cases and 3556 controls for hsa-mir-27a rs895819 polymorphism. The studies identified and their main characteristics are summarized in Table 1. Among these publications, there were two studies of European descent (Yang et al., 2010; Zhang et al., 2012), two study of Asian descent (Sun et al., 2010; Catucci et al., 2012). All of the cases were histologically confirmed as breast cancer or Gastric cancer. Controls were mainly healthy populations, and matched with age, sex, menopause status, or cancer-free.

Main results

The main results of this meta-analysis are shown in Table 2. When all the eligible studies were pooled into the

Table 1. Main Characteristics of Studies Included in This Meta-analysis

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Origin</th>
<th>Tumor type</th>
<th>Sample size (cases/controls)</th>
<th>Genotype (case/control)</th>
<th>Genotyping methods</th>
<th>HWE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun et al.</td>
<td>2010</td>
<td>Chinese</td>
<td>Gastric cancer</td>
<td>304/304</td>
<td>115/145 135/119 54/40</td>
<td>PCR-RFLP</td>
<td>Yes</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>2010</td>
<td>German</td>
<td>Breast cancer</td>
<td>1189/1416</td>
<td>576/605 486/660 127/151</td>
<td>TaqMan SNP assay</td>
<td>Yes</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>2011</td>
<td>Chinese</td>
<td>Breast cancer</td>
<td>245/243</td>
<td>60/75 144/109 41/59</td>
<td>PCR-RFLP</td>
<td>No</td>
</tr>
<tr>
<td>Catucci et al.</td>
<td>2012</td>
<td>Italian</td>
<td>Breast cancer</td>
<td>1025/1593</td>
<td>547/803 388/633 90/157</td>
<td>TaqMan SNP assay</td>
<td>No</td>
</tr>
</tbody>
</table>
Association Between the hsa-mir-27a Variant and Breast Cancer Risk: a Meta-analysis

Table 2. Associations of rs895819 and Cancer Risk

<table>
<thead>
<tr>
<th>No. of Comparisons</th>
<th>AG vs AA</th>
<th>P</th>
<th>GG vs AA</th>
<th>P</th>
<th>AG/GG vs AA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total F</td>
<td>4</td>
<td>0.95(0.90-1.01)</td>
<td>0.0005</td>
<td>0.94(0.80-1.11)</td>
<td>0.08</td>
<td>0.92(0.83-1.01)</td>
</tr>
<tr>
<td>R</td>
<td>4</td>
<td>1.07(0.80-1.44)</td>
<td>0.0004</td>
<td>0.98(0.75-1.29)</td>
<td>0.08</td>
<td>1.05(0.80-1.37)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian F</td>
<td>2</td>
<td>1.23(1.07-1.42)</td>
<td>0.66</td>
<td>1.25(0.88-1.78)</td>
<td>0.06</td>
<td>1.45(1.13-1.86)</td>
</tr>
<tr>
<td>R</td>
<td>2</td>
<td>1.52(1.16-1.98)</td>
<td>0.61</td>
<td>1.23(0.63-2.37)</td>
<td>0.06</td>
<td>1.45(1.13-1.86)</td>
</tr>
<tr>
<td>European F</td>
<td>2</td>
<td>0.90(0.84-0.96)</td>
<td>0.27</td>
<td>0.86(0.71-1.05)</td>
<td>0.8</td>
<td>0.84(0.75-0.94)</td>
</tr>
<tr>
<td>(Breast cancer) R</td>
<td>2</td>
<td>0.83(0.72-0.97)</td>
<td>0.2</td>
<td>0.86(0.71-1.05)</td>
<td>0.8</td>
<td>0.84(0.75-0.94)</td>
</tr>
<tr>
<td>Tumor type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast F</td>
<td>3</td>
<td>0.93(0.87-0.99)</td>
<td>0.005</td>
<td>0.86(0.72-1.03)</td>
<td>0.97</td>
<td>0.87(0.78-0.97)</td>
</tr>
<tr>
<td>R</td>
<td>3</td>
<td>0.98(0.73-1.32)</td>
<td>0.004</td>
<td>0.86(0.72-1.03)</td>
<td>0.97</td>
<td>0.92(0.74-1.14)</td>
</tr>
</tbody>
</table>

F, Fixed-effects model; R, Random-effects model; P, values for heterogeneity

In conclusion, this meta-analysis provided evidence that Hsa-mir-27a rs895819 polymorphism was associated with a decreased breast cancer risk compared with AA genotype. What’s more, we found that Asian carrying AG genotype of Hsa-mir-27a rs895819 polymorphism was associated with a decreased breast cancer risk compared with AA genotype, indicating that Hsa-mir-27a rs895819 polymorphism may play an important role in breast cancer development. However, we failed to find any association between rs895819 polymorphism and breast cancer risk in Europeans and Asian altogether.

We also failed to find any association between rs895819 polymorphism and all the cancers we analyzed in our meta-analysis.

What’s more, we found that Asian carrying AG genotype of Hsa-mir-27a rs895819 polymorphism was associated with an increased cancer risk (breast cancer and gastric cancer) compared with AA genotype. In fact, the number of Asian in our meta-analysis is so small that this conclusion may not very accurate.

Some limitations of this meta-analysis should be discussed. First, the number of studies included in the meta-analysis was not very large to perform subgroup analysis. Second, lack of available information prevented a more precise evaluation with adjusted ORs by age, menopausal status and express of ER/PR or Her2, etc. Third, there was no study of other population except Europeans and Asian.

In conclusion, this meta-analysis provided evidence that Hsa-mir-27a rs895819 polymorphism in Europeans carrying AG genotype was associated with a decreased breast cancer risk compared with AA genotype. Well-designed studies with larger sample size are of great value to confirm these findings.

Acknowledgements

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References


