INPLASY PROTOCOL

To cite: Zhou et al. Update on the Relationship Between the SLC4A7 variant rs4973768 and Breast Cancer risk: a systematic review and meta-analysis. Inplasy protocol 202320013. doi: 10.37766/inplasy2023.2.0013

Received: 03 February 2023

Published: 03 February 2023

Corresponding author:
YUHUI ZHOU

z1997156@163.com

Author Affiliation:
The First Affiliated Hospital of Xi'an Jiaotong University.

Support: **The First Affiliated Hospital of Xi'an Jiaotong University.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Update on the Relationship Between the SLC4A7 variant rs4973768 and Breast Cancer risk: a systematic review and meta-analysis

Zhou, YH[1]; Ma, XX[2]; SUN, JG[3].

Review question / Objective: **The aim of this meta-analysis was to get an updated opinion, which was about the role of the single nucleotide polymorphism (SNP) rs4973768 in the SLC4A7 gene played in the incident of breast cancer.**
Eligibility criteria: **The included criteria were formulated for this meta-analysis as following:(1) studies with both case and control groups;(2) studies assessing the relation between the SLC4A7 rs4973768 polymorphism and sensibility to breast cancer;(3) studies with sufficient information such as genotype frequency for results of odds ratios (ORs) and 95% confidence intervals (95% CIs); and (4) full-text articles of studies with human subjects. Studies meeting any one of the criteria were determined unqualified for this meta-analysis as following:(1) conference abstracts, comments, reviews, case reports, or editorials;(2) inadequate data for OR calculation;(3) no control group; and (4) animal studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 February 2023 and was last updated on 03 February 2023 (registration number INPLASY202320013).

INTRODUCTION

Review question / Objective: **The aim of this meta-analysis was to get an updated opinion, which was about the role of the single nucleotide polymorphism (SNP) rs4973768 in the SLC4A7 gene played in the incident of breast cancer.**

Condition being studied: **In the world, one of the most usual tumors in women is breast cancer, whose incidence rate accounts for 30% of female cancers in the USA, ranking first among female malignant tumors. The 2020 statistics of China's National Cancer Center reported that the number of new cases of female breast cancer was 416371, ranking first in the**

number of new cases of female cancer in China. Breast cancer is mostly sporadic, and some of them are hereditary. Its pathogenesis is not completely clear. A variety of gene changes produce abnormal gene products or product function changes, which can lead to breast cancer, so it is very important to find breast cancer susceptibility genes.

As a possible substrate of tyrosine kinase, SLC4A7 was proved to be down regulated in cell lines and neoplastic tissues. SLC4A7 rs4973768 existed in the 3'-UTR, whose accurate function has been still unclear. Since 2009, when it was first determined that this variant was associated with susceptibility to breast cancer, a large number of studies have successively investigated the association between rs4973768 and breast cancer risk; However, subsequent studies have yielded inconsistent results. In 2012, a study conducted a meta-analysis on the relationship between SLC4A7 rs4973768 and breast cancer. However, a number of new experiments have studied the relationship between the rs4973768 and breast cancer risk after 2012. Therefore, in order to further explore the relationship between rs4973768 and breast cancer risk, we conducted a meta-analysis incorporating relevant studies published before 2022 to accurately assess the relationship between them.

METHODS

Participant or population: The included criteria were formulated for this meta-analysis as following:(1) studies with both case and control groups;(2) studies assessing the relation between the SLC4A7 rs4973768 polymorphism and sensibility to breast cancer;(3) studies with sufficient information such as genotype frequency for results of odds ratios (ORs) and 95% confidence intervals (95% CIs); and (4) full-text articles of studies with human subjects. Studies meeting any one of the criteria were determined unqualified for this meta-analysis as following:(1) conference abstracts, comments, reviews, case reports, or editorials;(2) inadequate data for OR calculation;(3) no control group; and (4) animal studies.

Intervention: The allele T of SLC4A7 rs4973768 mutation.

Comparator: Not applicable.

Study designs to be included: Relevant studies were identified from digital databases such as Embase, PubMed, Medline, Cochrane Library, Google Scholar, WanFang, and Chinese National Knowledge Infrastructure (CNKI). Fixed- or random-effects models were used to calculated Odds ratios (ORs) with their corresponding 95% confidence intervals (95% CIs). The Q test and I2 statistic were used to inspect interstudy heterogeneity, and sensitivity analysis was implemented to test the statistical stability of the overall estimates. Egger's test was applied to inspect potential publication bias among the included studies.

Eligibility criteria: The included criteria were formulated for this meta-analysis as following:(1) studies with both case and control groups;(2) studies assessing the relation between the SLC4A7 rs4973768 polymorphism and sensibility to breast cancer;(3) studies with sufficient information such as genotype frequency for results of odds ratios (ORs) and 95% confidence intervals (95% CIs); and (4) full-text articles of studies with human subjects. Studies meeting any one of the criteria were determined unqualified for this meta-analysis as following:(1) conference abstracts, comments, reviews, case reports, or editorials;(2) inadequate data for OR calculation;(3) no control group; and (4) animal studies.

Information sources: A comprehensive writings search was applied in academic databases, including PubMed, Embase, Medline, Google Scholar, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang and different combinations of the keywords were used search, such as "BC, breast carcinoma or breast neoplasm" and "rs4973768 or SLC4A7". After reviewing the included

articles, further relevant articles were ascertained into our research.

Main outcome(s): The overall ORs reflected a positive correlation between theSLC4A7 rs4973768 polymorphism and susceptibility to breast cancer in five genetic comparisons of allele T vs. allele C (OR =1.1,95%CI =1.05–1.14,P=0.000), TT+CT vs. CC (OR =1.12,95%CI =1.06–1.18,P=0.000), TT vs. CC+CT (OR =1.1,95%CI =1.06–1.14,P=0.000), TT vs. CC (OR =1.17,95%CI =1.09–1.25,P=0.000), and CT vs. CC (OR =1.1,95%CI =1.04–1.16,P=0.001). The statistical Q test and I2 statistic revealed significant heterogeneity in the allele T vs. allele C comparison. After stratified by ethnicity, heterogeneity in Asian was substantial decreased (Ph=0.984, I2=0%); however, the heterogeneity was still existed in Caucasian population (Ph=0.083, I2=46.3%).

Quality assessment / Risk of bias analysis: Through the optical inspection of Egger's funnel plots with statistical consequences, potential publication bias among the contained studies could be judged. In our study, plot and p value (p>0.05) results of Egger's linear regression tests revealed significant publication bias were non-existent in all kinds of comparison. From the results of sensitivity analysis, we saw no material alterations existed in recalculated ORs when compared with the original ORs after deleting any single eligible study in all kinds of comparison, which implied that our results were dependable and firm.

Strategy of data synthesis: All data analysis were calculated in STATA software (version 17.0). The strength of the association between the SLC4A7 rs4973768 and breast cancer susceptiveness was determined by calculating pooled ORs and 95% CIs. The interstudy heterogeneity assumption was examined by means of χ2-based Q-statistic and I2 tests. If heterogeneity was calculated significantly (p 50%), the random-effects model would be used to get the summarized OR estimates in DerSimonian and Laird method; otherwise, the fixed-effects model would be was applied in Mantel-Haenszel method. Additionally, when the heterogeneity between studies was statistically significant, subgroup analysis would be applied to recognize potential causes of such heterogeneity. Egger's linear regression test was used to assess probable publication bias among the contained studies. The stability of the joint consequences was inspected by applying a sensitivity analysis, in which each of the contained studies was sequentially removed, and then summary ORs were recalculated to observe alterations between the original and reobtained ORs. P <0.05 was indicated as statistical significance.

Subgroup analysis: When significant heterogeneity existed in the comparisons, subgroup analysis was carried out, and the results demonstrated that racial difference could answer the significant heterogeneity of most or even all sources. After stratified by race, the heterogeneity of Asian was substantial decreased (Ph=0.984, I2=0%); but, the heterogeneity of Caucasian was still remained (Ph=0.083, I2=46.3%).

Sensitivity analysis: From the results of sensitivity analysis, we saw no material alterations existed in recalculated ORs when compared with the original ORs after deleting any single eligible study in all kinds of comparison, which implied that our results were dependable and firm.

Country(ies) involved: China.

Keywords: SLC4A7,rs4973768,Breast cancer, Risk.

Contributions of each author:
Author 1 - YUHUI ZHOU.
Email: z1997156@163.com
Author 2 - XIAOXIA MA.
Author 3 - JINGLAN SUN.