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Meta-analysis of Atherogenic Index of Plasma and other lipid parameters in relation to risk of type 2 diabetes mellitus

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ABSTRACT

Aims: Diabetic dyslipidemia is one of important complication of type 2 diabetes mellitus (T2DM). Blood lipid parameters (e.g., triglyceride, TG; total cholesterol, TC; high-density lipoprotein cholesterol, HDL-C; low-density lipoprotein cholesterol, LDL-C; Atherogenic Index of Plasma defined as lg(TG/HDL-C), AIP), are important indexes in predicting risk of T2DM. This study performed comprehensive meta-analyses to evaluate the powers of these indexes, especially for AIP, on predicting risk of T2DM.

Methods: We searched PubMed Database, China National Knowledge Infrastructure (CNKI) and Wanfang Database in February 2014 to identify eligible studies. Case–control studies that have mean baseline values of AIP were included. Random-effect models were used to pool the summary standardized mean difference (SMD) in meta-analysis.

Results: Fifteen eligible studies, with a total sample size of 4010, were included in meta-analysis. All these studies reported positive associations between AIP and T2DM. Moreover, the SMD for the AIP is 1.78 (95% confidence interval (CI): 1.04–2.52), which is higher than for other parameters (TG: 0.93, 95% CI: 0.78–1.09; TC: 0.46, 95% CI: 0.21–0.71; HDL-C: −0.89, 95% CI: −1.18 to −0.60; and LDL-C: 0.44, 95% CI: 0.11–0.77). Meta-analysis of association between BMI and T2DM gave a SMD of 0.85 (95% CI: 0.38 to 1.32).

Conclusions: The results suggest that lipid parameters have ability to reflect the risk of T2DM, but AIP may be more closely associated with the risk of T2DM. The current results suggest AIP may be used as a simple, easily calculated parameter in assessing the risk of T2DM.

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1. Introduction

Diabetic dyslipidemia is one of important complication of type 2 diabetes mellitus (T2DM). The alterations of blood lipid parameters, e.g., triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), are commonly detected in type 2 diabetic patients. Atherogenic Index of Plasma (AIP), the logarithm of molar ratio of TG to HDL-C, is a newly developed parameter, and could be used as a marker of plasma atherogenicity [1]. Previous studies reported that AIP is associated with T2DM [2–16]. However, the sample size is very limited in these individual studies. To date, no study has systematically evaluated and compared the power of the above T2DM-associated-parameters in predicting the risk to T2DM. Therefore, in this study we re-assessed the associations between AIP and risk of T2DM by conducting a meta-analysis with a large sample size ($N = 4010$). Meanwhile, we assessed associations of other blood lipid parameters (e.g., TG, TC, HDL-C and LDL-C) with risk of T2DM.

2. Methods

2.1. Study selection

We searched PubMed Database, China National Knowledge Infrastructure (CNKI) and Wanfang Database through February 2014 for relevant studies, using the terms *atherogenic index plasma*, *AIP*, *type 2 diabetes mellitus and diabetes*. The search was restricted to human studies. No language restrictions were imposed. In addition, we examined all references of related reviews and papers identified by the searching. No attempt was made to identify unpublished studies.

Studies were considered eligible for meta-analysis if (1) the study design was a case-control trial; (2) the ascertainment of T2DM was possible in all patients; (3) the mean (standard deviation, SD) value of AIP (in both cases and controls) was available.

2.2. Data abstraction

All data were abstracted with an electronic data-collection form. Study characteristics recorded were as follows: (1) first author's name, publication year, and study geographic region; (2) sample size of case and control group, sex distributions; (3) mean age or age range of participants; (4) baseline mean AIP, BMI, TG, TC, HDL-C, LDL-C and their corresponding SDs in each group, p value of each case–control group. If case or control group was categorized into more than one subgroup by some conditions, the mean baseline AIP, BMI, TG, TC, HDL-C, LDL-C for each group was calculated by combining the mean value from case or control groups, weighted by its proportion.

2.3. Statistical analysis

We first examined statistical heterogeneity across studies by calculating I^2 statistics. As in the systematic review, random-effects models were used to compute standardized mean difference (SMD) by pooling the data from case–control studies because of the significant statistical heterogeneity.

To assess potential publication bias, we constructed funnel plots for each outcome. In addition, the Begg rank correlation test and Egger linear regression test were employed to quantify this bias. We also conducted a sensitivity analysis to evaluate influence of each trial in merger of total results and test stability and reliability of the results. All analyses were performed using STATA version 12.0 (STATA Corp., College Station, TX). A P value less than 0.05 was considered statistically significant, except where otherwise specified.

3. Results

Fifteen published studies, including 1727 T2DM patients and 2283 controls, were identified from a full-text examination of 66 potentially relevant studies (Fig. 1). The characteristics and the measure parameters of the study participants are presented in Tables 1a and 1b.

Subjects with T2DM had significantly higher AIP values (SMD: 1.78; 95% CI: 1.04, 2.52; $p = 2.328E{-}6$; Fig. 2), compared with subjects without T2DM, and the heterogeneity was presented ($I^2 = 98.6\%$). We found no evidence of publication bias (Egger test $P = 0.611$). Our sensitivity analysis showed minimal influence on the combined results for single trial.

Among the included studies, 7 studies provided mean baseline values of BMI and their corresponding SDs. The patients with T2DM in these studies had significantly higher BMI values (SMD: 0.85; 95% CI: 0.38, 1.32; $p = 4.408E{-}4$; Fig. 3), compared with controls.

We also abstracted baseline mean TG, TC, HDL-C and LDL-C and their corresponding SDs. Summary estimates for the risk of T2DM are showed in Fig. 4. For the TG, meta-analysis in ten studies showed that the effect size increased greatly, compared with the participants in control groups (SMD: 0.93; 95% CI: 0.78, 1.09; $p = 7.522E{-}34$). For the TC, twelve studies remained in the meta-analysis, and the effect size marginally increased in case groups (SMD: 0.46; 95% CI: 0.21, 0.71; $p = 3.568E{-}4$). Meta-analysis performed in eleven studies for HDL-C data detected a significant reduction of the HDL-C value in patients, in comparison to the controls (SMD: −0.89; 95% CI: −1.18, −0.60; $p = 1.366E{-}9$). For the LDL-C, a small but significantly higher value was shown in patients, compared with the controls (SMD: 0.44; 95% CI: 0.11, 0.77; $p = 9.284E{-}3$; ten studies provided).

4. Discussion

Diabetic dyslipidemia, which is generally characterized by increased plasma TG, decreased HDL-C concentrations and a preponderance of small, dense low-density lipoprotein (sdLDL), is regarded as an important complication of T2DM in recent years. The "vicious cycle" hypothesis, dyslipidemia-insulin resistance-hyperinsulinemia vicious cycle, has been recently studied to find more evidence for preventing T2DM [17,18]. High TG levels may contribute to insulin resistance (IR) by competing with glucose for entering the cell that lead to impaired utilization of glucose oxidation. Hypertriglyceridemia often accompanies obesity, and declines in number