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The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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META-ANALYSIS

Coffee consumption and risk of type 2 diabetes mellitus in Asians: A meta-epidemiological study of population-based cohort studies

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Abstract

BACKGROUND

Previous systematic reviews have consistently reported that coffee consumption has a preventive effect on the occurrence of type 2 diabetes mellitus (T2DM). However, further evaluations between coffee consumption and the risk of T2DM in Asian populations are needed.

AIM

To conduct a meta-epidemiological study on systematic reviews evaluating the association between coffee consumption and the risk of T2DM in Asian people.

METHODS

The selection criterion was defined as a population-based prospective cohort study evaluating the association between coffee consumption and the risk of T2DM in Asian populations, reporting the adjusted relative risk (RR) and its 95% confidence interval (CI) for potential confounders. A fixed-effect model meta-analysis was applied to calculate the summary RR and its 95%CI in less than 50% of the I^2 value indicating the level of heterogeneity. A two-stage fixed-effects dose-response meta-analysis (DRMA) was performed to calculate the risk per unit dose (a cup per day).

RESULTS

A total of seven studies were selected in this meta-epidemiological study. The risk of T2DM in Asian populations was significantly reduced in the highest to the lowest dose group (summary RR = 0.73, 95%CI: 0.66-0.82; I^2 value = 0.0%). The DRMA showed that drinking one cup of coffee per day reduced the risk of T2DM in Asian populations by 8% (RR = 0.92, 95%CI: 0.90-0.95).

CONCLUSION

These findings support the conclusion that coffee consumption has a protective effect on the occurrence of T2DM in Asian men and women.

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Core Tip: Previous systematic reviews have consistently reported that coffee consumption has a preventive effect on the occurrence of type 2 diabetes mellitus (T2DM). However, differences in coffee consumption habits by region could create heterogeneity. This research aimed to conduct a meta-epidemiological study on systematic reviews evaluating the association between coffee consumption and the risk of T2DM in Asian populations. From a total of seven Asian cohort studies, it was concluded that coffee consumption has a protective effect on the occurrence of T2DM in Asian men and women.

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INTRODUCTION

The prevalence and incidence of type 2 diabetes mellitus (T2DM) has increased globally[1]. T2DM has a huge disease burden because of several cardiovascular, neuronal, renal, or ophthalmic complications[2].

Coffee consumption has been known to reduce the risk of T2DM since van Dam and Hu[3] reported it in 2005[3-8]. Further, Carlström and Larsson[8] reported an inverse association between coffee consumption and the risk of T2DM in Asian [summary relative risk (sRR) = 0.73, 95% confidence interval (CI): 0.64-0.82], European (sRR = 0.69, 95%CI: 0.62-0.75), and American (sRR = 0.74, 95%CI: 0.65-0.84) populations through a systematic review published in 2018. However, when analyzing the subgroups by geographical region, the I^2 values of the United States, Europe, and Asia were 73.8%, 46.8%, and 0.0%, respectively. Therefore, it can be inferred that the differences in coffee consumption habits by region could create heterogeneity. The Western Pacific region has the largest number of people with diabetes as reported by the International Diabetes Federation Diabetes Atlas[1]; therefore, further evaluations between coffee consumption and the risk of T2DM in Asian populations are needed.

In addition, the results of dose-response meta-analysis (DRMA) by sex as reported by Carlström and Larsson[8] showed that there was an indication of a stronger association in women (P for difference by sex = 0.03). Hence, it is necessary to determine whether there is a difference in the risk of T2DM between men and women in Asian populations according to coffee consumption.

Therefore, this research aimed to conduct a meta-epidemiological study on systematic reviews evaluating the association between coffee consumption and the risk of T2DM in Asian men and women.

MATERIALS AND METHODS

Selection strategies

The study subjects of the meta-epidemiological study were the original articles selected by previous systematic reviews[9,10]. Carlström and Larsson[8] selected five Asian cohort studies[11-15], with the latest year of publication in 2015[15]. Thus, it was necessary to include additional papers up to May 31, 2020. Hence, the "cited by" option provided by PubMed[16] was applied to make a list of papers citing the 31 papers selected in previous systematic reviews[4-8].

Papers were selected in the list according to the following criteria: (1) Population-based prospective cohort studies evaluating the association between coffee consumption and T2DM risk in the Asian population; and (2) Studies reporting the

adjusted RR and its 95%CI for potential confounders. Therefore, retrospective cohort studies, case-control studies, studies involving non-Asian populations, or studies that did not adjust for potential confounders were excluded.

Control of confounders

In the studies selected through the above selection processes, the level of adjusting smoking status (LAS) and level of adjusting alcohol intake (LAA) were evaluated by the levels reported by Thomas and Hodges[17], as smoking status and alcohol consumption are highly related to coffee consumption[17,18]. The low level was defined as adjusting for only status and the high level was defined as adjusting for intensity and status.

Statistical analysis

The RR and its 95%CI values adjusted for potential confounders in the highest *vs* lowest dose groups were extracted from each study for conducting a meta-analysis. The level of heterogeneity among the studies was evaluated as an I^2 value (%). A fixed-effect model was applied to calculate the sRR and its 95%CI in less than 50% of the I^2 value[19]. Subgroup analyses by sex (men, women), LAS (high, low), LAA (high, low), and family history of T2DM (FHX; yes, no) were conducted. The Egger test for small-study effects and funnel plots were performed to check for publication bias[20]. The non-parametric trim and fill analysis was performed to estimate the sRR reflecting publication bias[21].

In addition, a two-stage fixed-effects DRMA was performed to estimate the incidence risk *per* unit dose (a cup per day) considering the P value of the goodness-of-fit. The linear relationship was confirmed by testing the null hypothesis that the coefficients of the second and third splines were all equal to zero[22]. The fixed-effect meta-analysis, Egger's test, non-parametric trim and fill analysis, and two-stage fixed-effects DRMA were performed using metan, metabias, metatrim, and glst commands of STATA software, respectively (version 14.2, StataCorp, TX, United States). A P value of < 0.05 was considered statistically significant.

RESULTS

Final selection

A total of 560 papers cited 31 studies selected by previous systematic reviews until May 31, 2020. After applying the selection criteria, two new studies were selected[23,24]. Accordingly, a total of seven cohort studies were finally selected for the meta-analysis[11-15,23,24] (Figure 1). The distribution of these studies by nationality was four published in Japan, and one each in Singapore, Taiwan, and Korea. Seven studies had 12 cohorts by sex, including five men, five women, and two cohorts adjusted for sex. A total of 6348 T2DM cases developed in 141813 participants during the follow-up period. The results of evaluating LAS, LAA, and FHX in each study are shown in Figure 2.

Summary effect size

The risk of T2DM in Asian populations was significantly reduced in the highest coffee dose group compared to the lowest dose group (sRR = 0.73, 95%CI: 0.66-0.82; I^2 value = 0.0%) (Figure 2). As the funnel plot and Egger's test for small-study effects showed that a publication bias (P = 0.01) was present (Figure 3), a non-parametric trim and fill analysis was conducted. Furthermore, coffee consumption still prevented T2DM in Asian populations (sRR = 0.73, 95%CI: 0.54-0.91; P value of test for heterogeneity = 0.99).

The statistical significance of the preventive effect did not change in the results of subgroup analysis according to sex, LAS, LAA, or FHX (Table 1). The results of DRMA showed that drinking a cup of coffee per day reduced the risk of T2DM in Asian populations by approximately 8% (RR = 0.92, 95%CI: 0.90-0.95) with a linear relationship (Figure 4). In addition, men and women in Asia had a protective dose-response effect with statistical significance (Table 2).

DISCUSSION

The findings of this study can be summarized as follows: Coffee consumption could

Table 1 Summary relative risk and its 95% confidence intervals

Group		Summary relative risk (95% confidence intervals) [I-squared %]
All		0.73 (0.66-0.82) [0.0]
Sex	Men	0.76 (0.65-0.89) [0.0]
	Women	0.73 (0.59-0.90) [13.8]
Level of adjusting[1] tobacco smoking	High	0.72 (0.58-0.90) [21.0]
	Low	0.73 (0.63-0.84) [0.0]
Level of adjusting[1] alcohol drinking	High	0.72 (0.60-0.87) [0.0]
	Low	0.72 (0.60-0.87) [34.0]
Adjusting family history	Yes	0.72 (0.58-0.90) [21.0]
	No	0.73 (0.63-0.84) [0.0]

[1]High: Adjusted for intensity as well as status; Low: Adjusted for only status.

Table 2 Dose-response meta-analysis by the intaking unit (cup per day)

	Relative risk (95% confidence interval)	*P* value of heterogeneity	*P* value of non-linearity
All	0.92 (0.90-0.95)	0.42	0.31
Men	0.95 (0.91-0.98)	0.72	0.08
Women	0.89 (0.85-0.94)	0.40	0.56

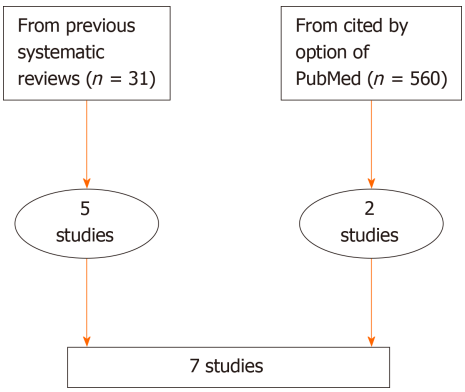


Figure 1 Flow chart of final selection.

decrease the occurrence of T2DM in Asian populations, and drinking a cup of coffee per day reduced the risk of T2DM in Asian population by approximately 8%.

Comparison with previous evidence

The results of this study consisting of 12 cohorts were consistent with the results of the study by Carlström and Larsson[8], which consisted of seven cohorts, in a meta-analysis comparing the highest to lowest coffee consumption. Women had a stronger association (11%) than men (5%) in the dose-response analysis per additional cup of coffee per day. In contrast to the results reported by Carlström and Larsson[8], this study showed statistically significant results in men. Hence, coffee consumption has a protective effect on the occurrence of T2DM in Asian men and women.

Natella and Scaccini[25] summarized the five effects of coffee in the modulation of diabetes mellitus risk and effects on glucose metabolism, thermogenic effects, antioxidant effects, anti-inflammatory effects, and chelating effects.

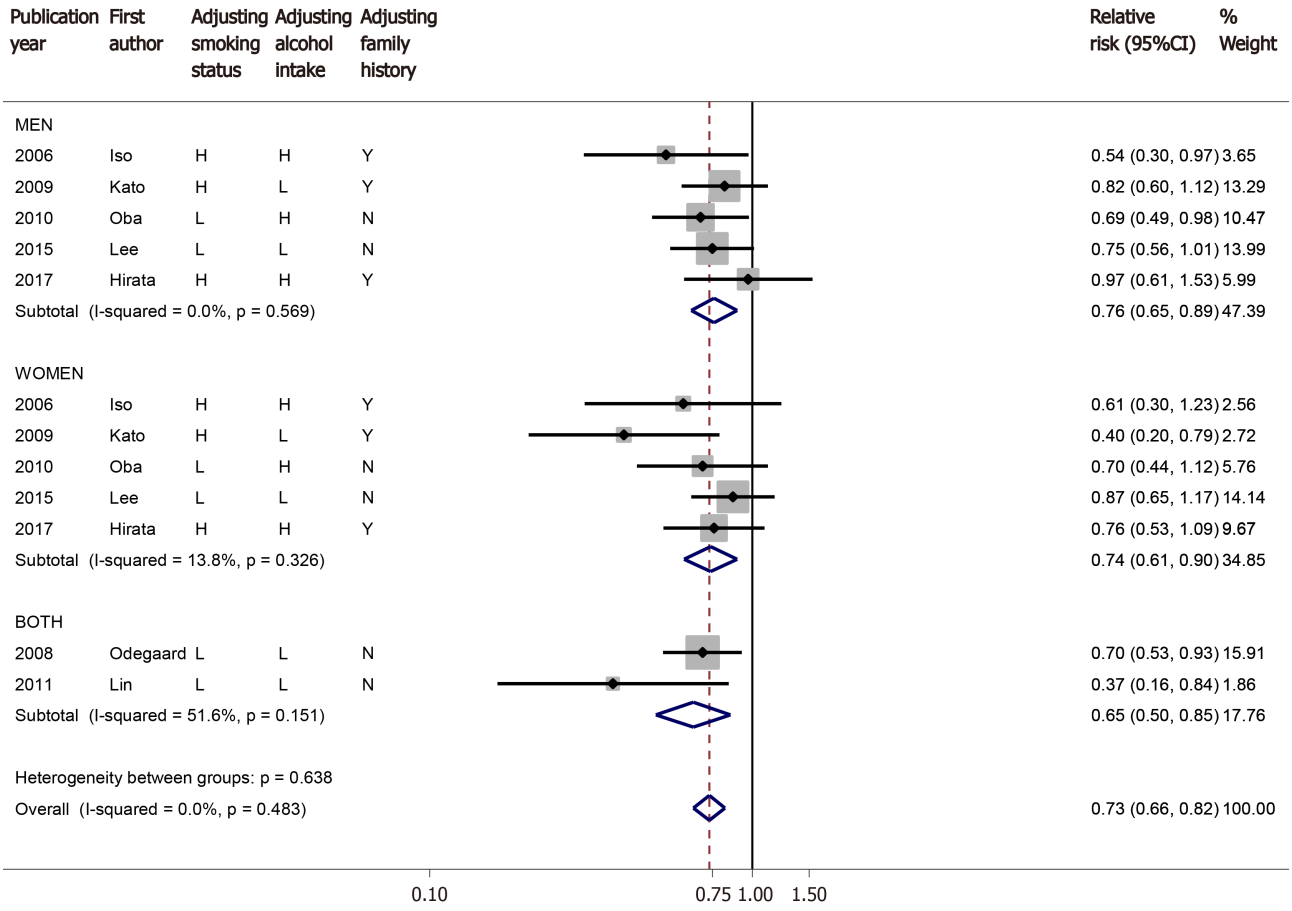


Figure 2 Forest plot to estimate summary relative risks by sex. CI: Confidence interval; H: High level; L: Low level; N: Not adjust; Y: Adjust.

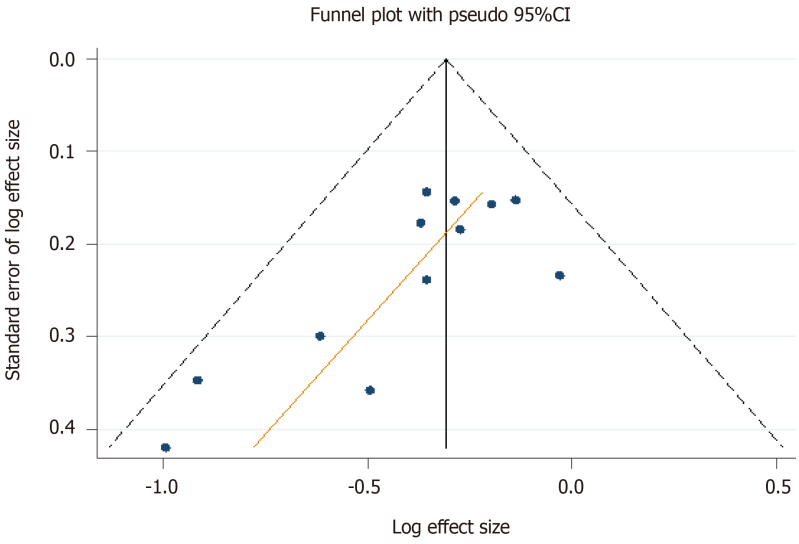


Figure 3 Funnel plot with Egger's test (*P* = 0.01).

Strengths

This meta-epidemiological study was able to find and include two cohort studies[23, 24], which should have been selected from existing systematic reviews. This was because they were cohort studies published before May 2017. It was re-confirmed that application of the "cited by" option of PubMed could be an effective search strategy [16].

As the Egger's test and funnel plot reported a publication bias, a non-parametric trim and fill analysis was conducted. Nevertheless, there was no change in the

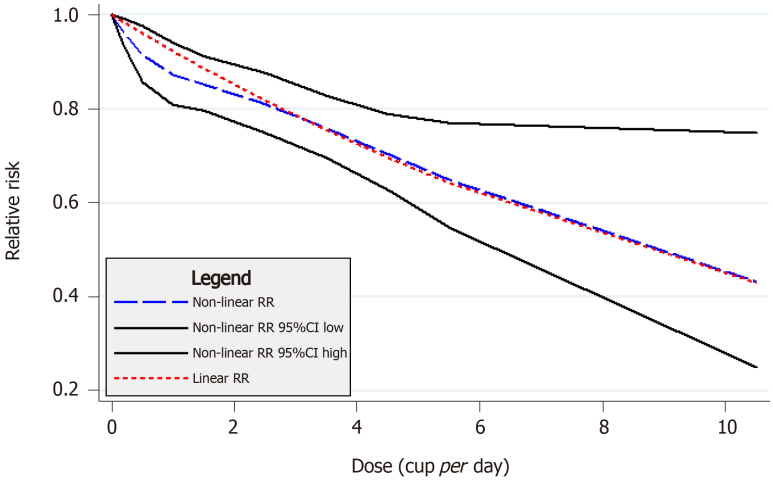


Figure 4 Dose-response meta-analysis in Asians. Relative risk and its low/high 95% confidence intervals. CI: Confidence interval; RR: Relative risk.

conclusion that coffee consumption reduced the risk of T2DM in Asian populations. As smoking and alcohol status would be highly related to coffee consumption, the LAS and LAA in each study were evaluated, and subsequently, subgroup analysis was performed. However, the preventive effect remained regardless of the LAS, LAA, and FHX. Therefore, coffee consumption had a protective effect on T2DM in Asian populations.

Limitations

The limitations of this meta-epidemiological study are the same as the limitations derived from the research design of prospective cohort studies that became the unit of meta-analysis.

Firstly, the information on coffee consumption and its quantity was usually obtained at the time of the cohort participation through a self-reported questionnaire. This should consider the possibility of measurement error[26]. The risk of T2DM decreased when the quantity of coffee consumption increased during the follow-up period, and the risk of T2DM increased when the quantity decreased[27]. Based on these findings, it can be inferred that the higher the coffee consumption, the more T2DM prevention, even if the coffee dose changes during the follow-up period.

In addition, when presenting the results obtained through follow-up, each cohort study had a different category of consumption and different references. Accordingly, the DRMA and meta-analysis using high *vs* low dose levels were conducted, and it was observed that coffee consumption prevented T2DM in Asian population.

CONCLUSION

This meta-epidemiological study confirmed that coffee consumption could prevent the occurrence of T2DM in Asian populations. Furthermore, the findings in the subgroup analyses by sex, LAS, LAA, and FHX showed the similar result consistently with statistical significance. In addition, the same results were obtained from the DRMA according to the daily consumption and the non-parametric trim and fill analysis in consideration of a publication bias. However, further studies are needed to investigate the preventive mechanism of coffee using a metabolomics study[28].

ARTICLE HIGHLIGHTS

Research background

The previous systematic reviews showed that an inverse association between coffee consumption and the risk of type 2 diabetes mellitus (T2DM).

Research motivation

While the differences in coffee consumption habits by region could create hetero-

geneity, further evaluations between coffee consumption and the risk of T2DM in Asian populations are needed.

Research objectives

The aimed to conduct a meta-epidemiological study to evaluate the association between coffee consumption and the risk of T2DM in Asian men and women.

Research methods

After selecting the studies meeting the selection criteria, a fixed-effect model meta-analysis and two-stage fixed-effects dose-response meta-analysis were performed.

Research results

Coffee consumption could decrease the occurrence of T2DM in the Asian population, and drinking a cup of coffee per day reduced the risk of T2DM in the Asian population by approximately 8%.

Research conclusions

This meta-epidemiological study concluded that coffee consumption could prevent the occurrence of T2DM in Asian populations.

Research perspectives

Further studies are needed to investigate the preventive mechanism of coffee using a metabolomics study.

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