INPLASY

Dipeptidyl Peptidase-4 Inhibitors and Coronary Plaque Burden in Diabetes: Meta-Analysis of Imaging-Based Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - This study received no external funding.

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 August 2025 and was last updated on 9 August 2025.

INTRODUCTION

Review question / Objective To evaluate the impact of dipeptidyl peptidase-4 inhibitors (DPP-4i) on coronary atherosclerosis in patients with diabetes or impaired glucose tolerance (IGT).

Condition being studied The PICO (population, intervention, comparison, outcome) setting of the current meta-analysis included: (1) P: patients with diabetes or IGT and coronary artery disease (CAD); (2) I: DPP-4i; (3) C: non-DPP-4i regimen; and (4) O: changes in percent atheroma volume (PAV) or total atheroma volume (TAV).

METHODS

Participant or population Human participants with diabetes or IGT and CAD.

Intervention DPP-4i.

Comparator Non-DPP-4i regimen.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria Studies were included based on the following criteria: (1) RCTs published in peer-reviewed journals with full-text availability; (2) comparison of DPP-4i therapy versus non–DPP-4i therapy; (3) reporting of changes in PAV or TAV from baseline to follow-up; and (4) use of intravascular ultrasound (IVUS) or three-dimensional quantitative coronary angiography (3D-QCA) to quantify atheroma burden. Exclusion criteria were non-randomized designs or absence of relevant primary outcomes.

Information sources We conducted a comprehensive literature search of PubMed, Embase, and Cochrane CENTRAL from database inception to July 31, 2025. Reference lists of selected articles were manually reviewed to identify additional eligible studies.

Main outcome(s) The primary outcomes were the changes in PAV and TAV between baseline and

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follow-up in participants receiving DPP-4i versus those on non-DPP-4i regimens.

Additional outcome(s) Secondary outcomes included changes in vessel metrics (vessel volume and lumen volume) and plaque composition (percent lipid, fibrotic, and calcified volume). Additional secondary outcomes comprised changes in laboratory parameters: lipid profiles [total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG)], glycemic control [glycated hemoglobin (HbA1c), fasting blood sugar (FBS)], and systemic inflammation [high-sensitivity C-reactive protein (hs-CRP)].

Quality assessment / Risk of bias analysis The risk of bias in the included trials was assessed using the Cochrane Risk of Bias 2.0 tool (RoB 2; London, UK), which evaluates six domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, selection of reported results, and overall bias. For intervention adherence, the per-protocol approach was adopted, in accordance with the designs and reporting patterns of the included studies. Publication bias was examined through funnel plot inspection and Egger's regression test when ≥10 datasets were available, as recommended by the Cochrane Handbook.

Strategy of data synthesis Owing to anticipated clinical and methodological heterogeneity, a random-effects model was used for all pooled analyses, conducted using Comprehensive Meta-Analysis software (version 3.0; Biostat, Englewood, NJ, USA). Statistical significance was set at a two-tailed $p < 0.05$. Effect sizes were calculated as Hedges' g with 95% confidence intervals and interpreted as small (0.2), moderate (0.5), or large (0.8), per standard thresholds. Heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Prediction intervals were used to assess the potential variability in treatment effects across future studies.

Subgroup analysis Meta-regression was performed to evaluate the influence of treatment duration on changes in plaque burden.

Sensitivity analysis Sensitivity analyses using a leave-one-out approach were performed to evaluate the robustness of results.

Country(ies) involved Taiwan.

Keywords dipeptidyl peptidase-4 inhibitors, coronary atherosclerosis, intravascular ultrasound, percent atheroma volume, meta-analysis.

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