

# INPLASY

## Effect of GLP-1 receptor agonist on cardiac remodelling: a systematic review and meta-analysis

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### ADMINISTRATIVE INFORMATION

**Support** - None.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202460063

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2024 and was last updated on 17 June 2024.

### INTRODUCTION

**Review question / Objective** Exploring the effects of GLP-1 receptor agonists on cardiac remodeling (LVEF  $\geq$  50%) in patients.

**Condition being studied** Cardiovascular disease is one of the most common causes of death globally, with approximately one-third of all deaths in China each year attributed to cardiovascular disease. Currently, the prevalence and mortality rates of cardiovascular disease are still on the rise, with the pressure and burden of cardiovascular disease increasing day by day, making prevention and treatment of cardiovascular disease urgent. Cardiac remodeling is the pathophysiological basis of many cardiovascular diseases such as heart failure and myocardial infarction, and the degree of cardiac remodeling is closely related to patient prognosis. Early intervention in cardiac remodeling has become a new strategy in clinical treatment. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are a class of drugs used to treat type

2 diabetes mellitus. These drugs stimulate the GLP-1 receptor, exerting an insulinotropic effect and resulting in glycemic control by promoting insulin secretion from the intestine. They are a type of insulin secretagogue medication that not only lowers blood glucose levels but also reduces body weight. In recent years, large-scale randomized controlled trials (RCTs) of GLP-1RAs have shown favorable effects on various adverse cardiovascular events, all of which are associated with cardiac remodeling. However, there is a lack of research on the impact of GLP-1RAs on cardiac remodeling and their underlying molecular mechanisms.

### METHODS

**Participant or population** Patients with left ventricular ejection fraction  $\geq$  50% with or without type 2 diabetes.

**Intervention** Use GLP-1RAs.

**Comparator** Do not use GLP-1RAs.

**Study designs to be included** Randomized controlled trial.

### Eligibility criteria

Inport:

- ① The exposure factor is the use of GLP-1 class drugs
- ② Application of non GLP-1 class drugs in the control group
- ③ Reactive cardiac remodeling related indicators
- ④ RCT research

Export:

- ① Case series/case reports/cross-sectional studies, literature reviews, systematic evaluations, and other non original studies
- ② There is relevant information, but the information is not sufficient to include in the analysis of the meeting summary
- ③ Animal experiments and other non clinical data
- ④ Repetitive literature/duplicate publications
- ⑤ Non English literature.

**Information sources** Retrieve all relevant literature on the relationship between GLP-1 receptor agonist application and cardiac remodeling from three major English electronic databases: PubMed, EMBASE, and Cochrane Library, without time or language limitations.

Steps Search terms

#1 "Exenatide" OR "liraglutide" OR "lixisenatide" OR "albiglutide" OR "dulaglutide" OR "semaglutide" OR "Glucagon-Like Peptide 1 Receptor Agonists" OR "Byetta" OR "Bydureon" OR "GLP" OR "Adlyxin" OR "Trulicity" OR "Ozempic" OR "Rybelsus"

#2 "cardi\*" OR "heart" OR "atri\*" OR "diastol\*" OR "systol\*" OR "ventricular remodeling" OR "CRR" OR "cardiac remodeling" OR "left ventricular dysfunction" OR "LVD"

#3 "LVEF" OR "ejection fraction" OR "EF" OR "left ventricular ejection fraction"

#4 "EDV" OR "end-diastolic volume" OR "EDD" OR "end-diastolic dimension" OR "LVEDD" OR "left ventricular end-diastolic" OR "LVEDV" OR "E/e" OR "E/Ea" OR "E/a" OR "early diastolic to late diastolic velocities ratio" OR "TRPV" OR "tricuspid regurgitation peak velocity" OR "LAVI" OR "left atrial volume index" OR "ESV" OR "end-systolic volume" OR "end-systolic dimension" OR "ESD" OR "LVESD" OR "left ventricular end-systolic" OR "LVESV" OR "left ventricular diameter" OR "left ventricular volume" OR "left ventricular mass index" OR "LVMI"

#5 #1 AND #2

#6 #1 AND #2 AND #3

#7 #1 AND #2 AND (#3 OR #4).

**Main outcome(s)** LVEF, LVESV, LVEDV, E/a, E/e and other indicators that can reflect cardiac remodeling.

**Quality assessment / Risk of bias analysis** This meta-analysis used the Cochrane bias risk assessment tool Risk of bias (ROB-2), which evaluates bias risk from six aspects: selection bias, implementation bias, measurement bias, follow-up bias, reporting bias, and other biases. Each aspect of the assessment is classified as high-risk, unclear, and low-risk [53]. Among the many types of research designs involved in clinical evidence-based medicine, randomized controlled trials (RCTs) serve as the "gold standard" for verifying the effectiveness of intervention measures and are an important component of producing high-quality meta-analyses. Therefore, the quality evaluation of RCTs is particularly important.

**Strategy of data synthesis** The data extracted from the selected data in this meta-analysis were processed using the STATA system evaluation software (version 13.0; Stata, University Station, Texas, USA). This study mainly deals with continuous moderating variables, and this econometric data is represented by the standardized mean difference (SMD) and its 95% confidence interval (CI). Choose random or fixed effects models based on the size of heterogeneity.

**Subgroup analysis** The heterogeneity included in the study was evaluated using a chi square test. When  $I^2 \leq 50\%$ , it is considered that the heterogeneity between studies is small. If the heterogeneity between studies is small, a fixed effects model is used for data analysis. If the statistical heterogeneity  $I^2$  is greater than 50%, a random effects model will be used for data analysis, while evaluating the sources of heterogeneity. When there is clinical heterogeneity, corresponding subgroup analysis should be conducted (such as subgroup analysis of studies with different follow-up times).

**Sensitivity analysis** Sensitivity analysis adopts a one by one exclusion method for evaluation. After removing the included studies one by one, the data of the other included studies are merged again to observe whether the results of the meta-analysis of the other studies have changed, in order to evaluate the stability of the research results. If there are low-quality studies included in the study, sensitivity analysis should be conducted again after removing the low-quality studies to evaluate whether the results of meta-analysis are affected by the low-quality studies.

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**Language restriction** Only English.

**Country(ies) involved** China.

**Keywords** GLP-1;GLP-1 receptor agonists;  
Cardiac remodeling; Cardiac function.

**Contributions of each author**

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