1-Endocrine aspects of metabolic dysfunction-associated steatotic liver disease (MASLD): Beyond insulin resistance

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Abstract

While the association of metabolic dysfunction-associated steatotic liver disease (MASLD) with obesity and insulin resistance is widely appreciated, there are a host of complex interactions between the liver and other endocrine axes. While it can be difficult to definitively distinguish direct causal relationships and those attributable to increased adipocyte mass, there is substantial evi-dence of the direct and indirect effects of endocrine dysregulation on the severity of MASLD, with strong evidence that low levels of growth hormone, sex hormones, and thyroid hormone promote the development and progression of disease. The impact of steroid hormones, e.g. cortisol and dehydroepiandrosterone, and adipokines is much more divergent. Thoughtful assessment, based on individual risk factors and findings, and management of non-insulin endocrine axes is essential in the evaluation and management of MASLD. Multiple therapeutic options have emerged that leverage various endocrine axes to reduce the fibroinflammatory cascade in MASH.

Keywords

Author Keywords

MASLDendocrine mediatorsMASH

Keywords Plus

HORMONE-BINDING GLOBULININDUCED NONALCOHOLIC STEATOHEPATITISPOLYCYSTIC-OVARY-SYNDROMEEARLY BREAST-CANCERFATTY LIVERHEPATIC STEATOSISGROWTH-HORMONEPOSTMENOPAUSAL WOMENTESTOSTERONE REPLACEMENTAROMATASE INHIBITORS

2-Association of Insulin Resistance With Cardiovascular Disease and All-Cause Mortality in Type 1 Diabetes: Systematic Review and Meta-analysis

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By Sun, R (Sun, Rui) [1] ; Wang, JX (Wang, Jianxin) [2] , [3] ; Li, M (Li, Meng) [1] , [4] , [5] ; Li, JE (Li, Jingen) [1] ; Pan, Y (Pan, Yi) [1] ; Liu, BR (Liu, Birong) [1] ; Lip, GYH (Lip, Gregory Y. H.) [4] , [5] , [6] ; Zhang, LJ (Zhang, Lijing) [1] (provided by Clarivate) **Source DIABETES CARE Volume 47 Issue 12 DOI 10.2337/dc24-0475 Published DEC 2024 Indexed 2025-01-05 Document Type Review**

Abstract

OBJECTIVE The association of insulin resistance (IR) with cardiovascular disease (CVD) and all-cause mortality in type 1 diabetes (T1D) remains unclear.PURPOSE To investigate whether IR is associated with CVD and all-cause mortality among individuals with T1D.DATA SOURCES PubMed, Embase, and the Cochrane Library databases were searched from inception to 31 October 2023.STUDY SELECTION Observational studies reporting the associations between IR, as calculated by the estimated glucose disposal rate (eGDR), and the risk of CVD and all-cause mortality in individuals with T1D were eligible for inclusion.DATA EXTRACTION Data from eight selected studies were extracted, pooled by random-effects models, and results are presented as hazard ratios (95% CIs).DATA SYNTHESIS Eight studies involving 21,930 individuals were included, of which five studies involving 19,960 individuals with T1D reported the risk of CVD. During a median follow-up of 10 years, there were 2,149 cases of incident CVD. The pooled hazard ratio for composite CVD outcome per 1-unit increase in the eGDR index was 0.83 (95% CI 0.78-0.90, I2 = 58.9%). Five studies involving 19,403 individuals reported the risk of all-cause mortality. During a median follow-up of 10 years, 1,279 deaths were observed. The pooled hazard ratio for all-cause mortality per 1-unit increase in the eGDR index was 0.84 (95% CI 0.81-0.87, I2 = 0%).LIMITATIONS The small number of available studies restricted our ability to perform meta-regression analyses or more detailed subgroup analyses.CONCLUSIONS IR, as calculated by the eGDR, may be an additional risk factor for CVD and all-cause mortality in T1D.

Keywords

Keywords Plus

GLUCOSE DISPOSAL RATEMETABOLIC SYNDROMEHEART-FAILURERISKCOMPLICATIONSADOLESCENTSCHILDRENOBESITYEVENTS

3- Insulin resistance assessed by estimated glucose disposal rate and risk of incident cardiovascular diseases among individuals without diabetes: findings from a nationwide, population based, prospective cohort study

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By Zhang, ZL (Zhang, Zenglei) [1] ; Zhao, L (Zhao, Lin) [1] ; Lu, YT (Lu, Yiting) [1] ; Xiao, Y (Xiao, Yan) [1] ; Zhou, XL (Zhou, Xianliang) [1] (provided by Clarivate) **Source CARDIOVASCULAR DIABETOLOGY Volume 23 Issue 1 DOI 10.1186/s12933-024-02256-5 Article Number 194 Published JUN 6 2024 Indexed 2024-06-21 Document Type Article**

Abstract

Background Recent studies have suggested that insulin resistance (IR) contributes to the development of cardiovascular diseases (CVD), and the estimated glucose disposal rate (eGDR) is considered to be a reliable surrogate marker of IR. However, most existing evidence stems from studies involving diabetic patients, potentially overstating the effects of eGDR on CVD. Therefore, the primary objective of this study is to examine the relationship of eGDR with incidence of CVD in non-diabetic participants. Method The current analysis included individuals from the China Health and Retirement Longitudinal Study (CHARLS) who were free of CVD and diabetes mellitus but had complete data on eGDR at baseline. The formula for calculating eGDR was as follows: eGDR (mg/kg/min) = 21.158 - (0.09 x WC) - (3.407 x hypertension) - (0.551 x HbA1c) [WC (cm), hypertension (yes = 1/no = 0), and HbA1c (%)]. The individuals were categorized into four subgroups according to the quartiles (Q) of eGDR. Crude incidence rate and hazard ratios (HRs) with 95% confidence intervals (CIs) were computed to investigate the association between eGDR and incident CVD, with the lowest quartile of eGDR (indicating the highest grade of insulin resistance) serving as the reference. Additionally, the multivariate adjusted restricted cubic spine (RCS) was employed to examine the dose-response relationship. Results We included 5512 participants in this study, with a mean age of 58.2 +/- 8.8 years, and 54.1% were female. Over a median follow-up duration of 79.4 months, 1213 incident CVD cases, including 927 heart disease and 391 stroke, were recorded. The RCS curves demonstrated a significant and linear relationship between eGDR and all outcomes (all P for non-linearity > 0.05). After multivariate adjustment, the lower eGDR levels were founded to be significantly associated with a higher risk of CVD. Compared with participants with Q1 of eGDR, the HRs (95% CIs) for those with Q2 - 4 were 0.88 (0.76 - 1.02), 0.69 (0.58 - 0.82), and 0.66 (0.56 - 0.79). When assessed as a continuous variable, per 1.0-SD increase in eGDR was associated a 17% (HR: 0.83, 95% CI: 0.78 - 0.89) lower risk of CVD, with the subgroup analyses indicating that smoking status modified the association (P for interaction = 0.012). Moreover, the mediation analysis revealed that obesity partly mediated the association. Additionally, incorporating eGDR into the basic model considerably improve the predictive ability for CVD. Conclusion A lower level of eGDR was found to be associated with increased risk of incident CVD among non-diabetic participants. This suggests that eGDR may serve as a promising and preferable predictor and intervention target for CVD.

Keywords

Author Keywords

Insulin resistanceCardiovascular diseasesEstimated glucose disposal rateNon-diabetesPredictive performance

Keywords Plus
ALL-CAUSE MORTALITYGLOBAL BURDENHYPERGLYCEMIAASSOCIATIONTOLERANCE