ISSN 1948-9358 (online)

World Journal of *Diabetes*

World J Diabetes 2024 November 15; 15(11): 2157-2271

Published by Baishideng Publishing Group Inc

World Journal of Diabetes

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Peer Review of *World Journal of Diabetes*, Dimiter Avtanski, PhD, Director, Endocrine Research Laboratory, Friedman Diabetes Institute, Lenox Hill Hospital, New York, NY 10022, United States. davtanski@northwell.edu

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INDEXING/ABSTRACTING

The *WJD* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJD* as 4.2; JIF without journal self cites: 4.1; 5-year JIF: 4.2; JIF Rank: 40/186 in endocrinology and metabolism; JIF Quartile: Q1; and 5-year JIF Quartile: Q2.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Diabetes

ISSN
ISSN 1948-9358 (online)

LAUNCH DATE
June 15, 2010

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Lu Cai, Md. Shahidul Islam, Michael Horowitz

EDITORIAL BOARD MEMBERS
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PUBLICATION DATE
November 15, 2024

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World Journal of Diabetes

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World J Diabetes 2024 November 15; 15(11): 2242-2244

DOI: 10.4239/wjd.v15.i11.2242

ISSN 1948-9358 (online)

LETTER TO THE EDITOR

Atrial fibrillation and prediabetes: Interplay between left atrium and systemic diseases

Ming-Jui Hung

Specialty type: Endocrinology and metabolism

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Li CP

Received: July 18, 2024
Revised: September 10, 2024
Accepted: September 18, 2024
Published online: November 15, 2024
Processing time: 89 Days and 20.7 Hours

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Abstract

Atrial fibrillation (AF) is associated with multiple other comorbidities, *i.e.* multimorbidity. Prediabetes is one of the multiple comorbidities observed in patients with AF, whereby these two disease entities share the same pathophysiological mechanisms, namely oxidative stress and inflammation. Although prediabetes is reported to have a negative impact on major adverse cardiac or cerebrovascular events in hospitalized AF patients, information about the interactions between prediabetes and AF remains inconsistent. A more in-depth exploration of pathophysiology and more comprehensive prospective clinical studies of AF and diabetes would provide a thorough understanding of the timing of events and further treatment strategies. Deeper investigations are needed to clarify the interactions and causal relationships between AF and prediabetes.

Key Words: Atrial fibrillation; Endothelial dysfunction; Inflammation; Prediabetes; Stroke

Core Tip: Atrial fibrillation (AF) and prediabetes share the same pathophysiological mechanisms, namely oxidative stress and inflammation. Batta *et al* commented on an article published recently regarding their negative impact on major adverse cardiac or cerebrovascular events in hospitalized AF patients. Further investigations are needed to clarify the interactions and causal relationships between AF and prediabetes.

Citation: Hung MJ. Atrial fibrillation and prediabetes: Interplay between left atrium and systemic diseases. *World J Diabetes* 2024; 15(11): 2242-2244
URL: https://www.wjgnet.com/1948-9358/full/v15/i11/2242.htm
DOI: https://dx.doi.org/10.4239/wjd.v15.i11.2242

TO THE EDITOR

I read with great interest a recent letter to the editor by Batta *et al*[1] in which they commented on a retrospective study about the impact of prediabetes on hospitalized atrial fibrillation (AF) patients[2]. The study found that prediabetes is negatively associated with major adverse cardiac or cerebrovascular events in hospitalized patients with AF. Batta *et al*[1] applauded the use of one of the largest datasets obtained from the national inpatient sample (2019) in the United States, adding that it provided further evidence of the association between prediabetes and AF-related hospitalization. The study's results are in line with other studies[3,4] which suggest that hyperglycemia, irrespective of prediabetes or diabetes, predicts adverse cardiac or cerebrovascular events, including myocardial infarction, heart failure, and stroke in AF patients. The authors[2] postulated some possible mechanisms to explain the association of cardiac or cerebrovascular events with prediabetes and AF, such as endothelial dysfunction, chronic inflammation, and oxidative stress.

However, Batta *et al*[1] also noted that there are some issues that needed to be addressed in that study[2]. These are: (1) Prediabetes is not clearly defined in the study; (2) Insufficient outcome comparisons with diabetes; (3) The role of metformin is unknown; and (4) The impact of reversion to normoglycemia is not addressed. These issues, as pointed out by Batta *et al*[1] are quite important in that the unclear definitions used, the insufficient group comparisons and the retrospective study design might produce different results after clear definitions are used, enough groups are compared, and a prospective study design is adopted. I concur with the view of Batta *et al*[1] that prospective cohort studies or randomized controlled trials would provide some deeper insights and conclusions about the complex relationship between prediabetes, diabetes, and AF. This would further promote our understandings about the natural course of cardiac or cerebrovascular events and the dynamic progression from normoglycemia through prediabetes to diabetes.

Recently, a different result was reported regarding the impacts of prediabetes on prognosis in AF patients. Ledo Piñeiro *et al*[5] performed a retrospective cohort study of 2993 non-diabetic AF patients. They evaluated the primary outcomes of ischemic stroke, myocardial infarction, and major bleeding during a median follow-up of 4.12 years and compared between normoglycemic and prediabetic groups. They found no association between glycated hemoglobin and worse prognosis in the prediabetic AF patients. Therefore, a prospective cohort study or randomized controlled trial is necessary to clarify the natural course of prediabetes in different clinical settings.

Interestingly, Herman[6] has offered a new perspective. They observe that the term "prediabetes" is not precise enough to describe a medical condition because it implies that individuals who have prediabetes will eventually develop diabetes, and those who do not have prediabetes will not develop diabetes in the future. Herman[6] points out that differentiating the risk of developing diabetes in the future based on a single blood test for glucose is suboptimal, because the process of progression is along a continuum. They therefore suggest using multi-variable models, including glycemia measurements and sociodemographic and clinical information to estimate an individual's risk, instead of using the mono-variable term "prediabetes". Intervention for patients who are at higher risk would be more effective and most cost-efficient in changing the individual's outcome.

While the overall cardio- and cerebro-protective benefits of prediabetes management outweigh the management-related costs, it is also important to prevent cardiac or cerebrovascular events in AF patients. Given the points raised by Batta *et al*[1], the issues of prediabetes and AF need more in-depth investigations in order to provide more effective and more cost-efficient strategies in public health management.

FOOTNOTES

Author contributions: Hung MJ contributed solely to design, data collection, drafting article and final approval of article.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

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S-Editor: Fan M
L-Editor: A
P-Editor: Wang WB

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