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ABOUT COVER

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AIMS AND SCOPE

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.

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

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Atrial fibrillation and prediabetes: A liaison that merits attention!

Akash Batta, Juniali Hatwal

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**Core Tip:** Atrial fibrillation (AF) and prediabetes share common pathophysiological mechanisms with endothelial dysfunction and inflammation playing a key role. The resultant vicious cycle which sets in culminates in higher atherogenicity and thermogenicity of the vascular system resulting in increased major adverse cardiac or cerebrovascular event (MACCE) events. However, the same has not convincingly been verified in real-world settings. In the recent retrospective study by Desai et al amongst AF patients being admitted to hospitals following MACCE, prediabetes emerged as an independent risk factor for MACCE after adjusting for all confounding variables. However, certain questions like the role of metformin, quantifying the risk for MACCE amongst prediabetes compared to diabetes, the positive impact of reversion to normoglycemia remain unanswered. We provide our insights and give future directions for dedicated research in this area to clarify the exact relationship between the two.

Abstract

Atrial fibrillation (AF) and prediabetes share common pathophysiological mechanisms with endothelial dysfunction and inflammation playing a key role. The resultant vicious cycle which sets in culminates in higher atherogenicity and thermogenicity of the vascular system resulting in increased major adverse cardiac or cerebrovascular event (MACCE) events. However, the same has not convincingly been verified in real-world settings. In the recent retrospective study by Desai et al amongst AF patients being admitted to hospitals following MACCE, prediabetes emerged as an independent risk factor for MACCE after adjusting for all confounding variables. However, certain questions like the role of metformin, quantifying the risk for MACCE amongst prediabetes compared to diabetes, the positive impact of reversion to normoglycemia remain unanswered. We provide our insights and give future directions for dedicated research in this area to clarify the exact relationship between the two.
We read with great interest the recent retrospective study by Desai et al.[1] amongst atrial fibrillation (AF) patients being admitted to hospitals following a major adverse cardiac or cerebrovascular event (MACCE). They looked into various risk factors leading to MACCE amongst AF patients, focusing primarily on the impact of prediabetes on adverse outcomes. The study is very much relevant in clinically practice as roughly 20% of all AF patients have concomitant prediabetes[2]. The authors deserve credit in analyzing a large database and making relevant conclusions which are likely to have a bearing in our approach to AF management.

In this study, the authors highlighted the negative impact of prediabetes in AF patients with prediabetes emerging as an independent risk factor for MACCE after adjusting for all confounding variables. The study indeed comes out as one of largest to date which supports a significant association between prediabetes and MACCE amongst AF patients.

The results of this study are in agreement with prior available data which supports dysglycemia (encompassing prediabetes and diabetes) as a strong risk factor for complications including heart failure, stroke, dementia and myocardial infarction amongst AF patients[2-5]. The basis of this is the common pathophysiology of the two which revolves around endothelial dysfunction and inflammation. The resultant vicious cycle which sets in culminates in a higher atherogenicity and thermogenicity of the vascular system resulting in increased MACCE events[6,7]. There is emerging evidence that the pathophysiology of prediabetes is identical to diabetes and it is often closely linked to multiple cardiovascular risk factors including obesity, dyslipidemia and metabolic syndrome. Understandably, it is associated with worse prognosis compared to normoglycemia independent of AF[8]. While the negative impact of prediabetes on MACCE is somewhat evident, the impact of reversion to normoglycemia on MACCE remains unclear.

The index study although appropriately highlights the impact of prediabetes on MACCE in AF, there are certain issues which have largely gone unattended. We believe some of our insights would help the authors and other researchers delve deeper which would enable us to get a more pellucid look at the relationship of these entities. Firstly, the definition of prediabetes used is not mentioned. The variable definitions do not necessarily correlate similarly with outcomes and thus far in clinical trials, the world health organization: Fasting and 2-hour post glucose load definitions have the highest strength of association with worse outcomes compared to American diabetes association blood glucose and HbA1c based definitions[9]. Hence, the definition used in this study becomes relevant. Secondly, the authors could have analyzed the diabetes cohort as well which would have helped in comparing the odds ratio of MACCE in prediabetes and diabetes compared to normoglycemia. Another possibly way could have been to stratify the population according to the HbA1c levels which again would have clarified the strength of association of dysglycemia with MACCE across the entire spectrum of patients ranging from normal levels to overt diabetes. The authors have not specified the timeline of diagnoses of prediabetes in relation to the MACCE and AF. This is necessary to understand when prediabetes starts to influence outcomes amongst AF patients. Thirdly, the impact of metformin use amongst prediabetics should have been looked at. Going by the data, it is expected that 3%-10% of all prediabetic patients use metformin to delay the progression to diabetes[10]. There is paucity of clear evidence in this regard and hence such a data would have helped clarify the role of metformin in this group of patients.

Since glycemic status of an individual in widely variable, likewise amongst prediabetes, the transition to normoglycemia or overt diabetes in not uncommon. The dynamic nature of this parameter hence cannot be completely accounted for in a retrospective study. Further, the retrospective study design is inherently prone to biases which are likely to influence the result and limit the generalizability of this study. This makes a strong case for larger prospective cohort studies and randomized trials which would further clarify the precise relationship between prediabetes and MACCE amongst AF patients by limiting the biases. Apart from these concerns, the readers must realize that the index study only analyses the data for hospitalized patients which were discharged subsequently. Since the vast majority of AF patients are ambulatory without prior MACCE related hospitalization, the findings of this study may not hold true for this group of patients.

Once again, we congratulate the authors for analyzing their large data set and providing key results for a major public health problem. Their findings hold great significance and provides insights on the negative impact of prediabetes in AF. We hope that our thoughts stimulate and draw the attention of researchers around the world to delve deeper into this field enabling us to better understand this complex relationship in the near future.

**FOOTNOTES**

**Author contributions:** Batta A designed, supervised, revised and approved the article; Hatwal J wrote the initial draft and revised the article; All authors have read and approved of the final version of the article.

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