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PEER-REVIEW REPORT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 116115

Title: Discriminating Diabetes Mellitus from Single-Lead ECG Using Machine Learning and Multinomial Regression

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08588323
Position: Peer Reviewer
Academic degree and professional title: PhD, Postdoc
Reviewer's Country/Territory: China
Author's Country/Territory: Russia

Manuscript submission date: 2025-11-02

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-11-06 07:11

Reviewer performed review: 2025-11-14 08:20

Review time: 8 Days and 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **No** Do authors' affiliations correspond to the content of the manuscript? **Yes** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes** Are the Key Words complete? **Yes**

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	Is the content of the Introduction adequate? **Yes** Is the content of the Materials and Methods complete? **No** Is the description of the experiments clear and complete? **No** Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable** Are the experimental data of the Results true and reliable? **Not Applicable** Are the quality and resolution of the images up to standard? **Not Applicable** Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes** Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes** Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes** Is the content of the Discussion reasonable? **Yes** Is the Conclusion reasonable? **Yes** Are all references necessary and reasonable? **Yes** Do authors omit important references? **No** Are all references related to the topic of the manuscript? **Yes** Do authors only cite their own earlier publications? **No** Is the manuscript's text correct, concise, and clear? **No** Will the manuscript's content be of interest to readers? **Yes** Are additional experiments needed for the study? **No**

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	Does the research scope comply with ethics? **Yes**
Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This study investigates the use of single-lead ECG and machine-learning models to detect and classify diabetes mellitus (type 1, type 2, and non-diabetic states). The topic is novel and clinically relevant, yet several critical aspects of study design, data description, and presentation require clarification before the findings can be properly interpreted：

1. Diagnostic Standards for Diabetes Mellitus

The manuscript does not specify how diabetes and its subtypes were diagnosed or

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confirmed. It is essential to state whether the diagnostic criteria followed ADA, WHO, or national guidelines and which tests (fasting plasma glucose, OGTT, HbA1c, medical record diagnosis) were used. Without these details, the reliability of the diagnostic labels used for model training and validation cannot be assessed.

2. Enrollment Strategy

The inclusion process remains unclear. Please indicate whether all eligible patients were consecutively enrolled during the study period or if the sample was selected or filtered (e.g., only those with complete ECG and glucose data). This information is critical to evaluate representativeness and potential selection bias.

3. Non-Inclusion vs. Exclusion Criteria

The current distinction between "Non-Inclusion" and "Exclusion" criteria is unnecessary and confusing, as both indicate reasons for not including participants. These should be merged into a single Exclusion Criteria section to avoid redundancy.

4. Section Structure

The paragraph beginning with "The patients underwent a comprehensive examination, including:" follows immediately after the exclusion list, which makes it appear to be part of the exclusion criteria. Adding a clear sub-heading such as "Clinical Assessment" or "Baseline Evaluation" would improve readability and logical flow.

5. Title Accuracy vs. Model Functionality

The title "Discriminating Type 1 and Type 2 Diabetes from Single-Lead ECG Using Machine Learning" implies that the model distinguishes between T1DM and T2DM. In fact, the model primarily discriminates between diabetic vs. non-diabetic states, with limited performance in differentiating T1DM from T2DM (AUC = 0.69). Consider revising the title and abstract to reflect the true scope and strength of the model.

6. Timing of ECG Acquisition

It is unclear whether ECG recordings were obtained before or after diabetes diagnosis. If

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ECGs were collected after confirmed diagnosis, the model reflects secondary electrophysiological changes caused by established disease rather than early screening potential. This limitation should be clarified and discussed.

7. Potential Confounding Cardiac Conditions

The study does not address whether patients with arrhythmias, ischemic heart disease, cardiomyopathies, or other ECG-altering disorders were excluded or adjusted for. These comorbidities can strongly influence ECG features and may confound model performance. Please clarify how such conditions were handled.

8. Structure of Discussion and Conclusion

The last paragraph of the Discussion begins with "In conclusion…" and repeats the statements in the formal Conclusion section. This redundancy can be avoided by merging or re-phrasing the final paragraph so that the main conclusions are only presented once in the designated Conclusion section.

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Reviewer's code: 08478544
Position: Peer Reviewer
Academic degree and professional title: Academic Fellow, Assistant Professor, Clinical Assistant Professor (Honorary), MD
Reviewer's Country/Territory: Türkiye
Author's Country/Territory: Russia

Manuscript submission date: 2025-11-02

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-11-13 06:16

Reviewer performed review: 2025-11-14 21:27

Review time: 1 Day and 15 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **Yes** Do authors' affiliations correspond to the content of the manuscript? **Yes** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes**

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	Does the research scope comply with ethics? **Yes**
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

I had the opportunity to review the article titled "Discriminating Type 1 and Type 2 Diabetes from Single-Lead ECG Using Machine Learning and Multinomial Regression." I congratulate the authors on their meticulous work. Overall, the article is well-written, but I have some suggestions for revision. These suggestions are listed below.

- Abstract

The running title does not reflect the title of the article. Changing the running title might

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be a good idea.

Keywords like ''Prevalence, Cardiovascular disease, and Metabolic syndrome'' can be deleted. Too many keywords have been typed.

- Introduction

The Introduction section is well-organized. The literature support, the purpose of the article, and any gaps in the literature are well explained. I have no additional suggestions or criticisms for this section.

Materials and Methods

The biggest shortcoming of this section is that the diagnostic criteria for DM are not specified. Furthermore, the classification of patients diagnosed with DM is not specified. The results share the prevalence of coronary artery disease. However, the methodology does not specify how CAD is diagnosed. A section titled "Definition" should be created, and these definitions should be added.

The study describes the use of artificial intelligence to diagnose and even type DM. However, this section should explain the AI's algorithm for making this distinction. Furthermore, the potential pathophysiological explanation should also be stated.

Adding the Clinical trial number URL to the methodology may make it easier for the reader.

I think that the statistical methods used in the post-hoc analyses of ANOVA and Kruskal-Wallis tests should be specified.

- Results

Table 1 needs significant revisions. There are numerous abbreviations, none of which have explanations. Only p-values are listed, but no information is provided on the nature of the differences between groups. I believe Table 1 needs to be rewritten. To be honest, I didn't understand anything from Table 1.

Figure 1 illustrates the differences between groups. I prefer using precise numbers in the

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table rather than this diagram. Exact numbers should be presented rather than large and small figures and estimates.

An examination of Table 2 reveals that the regression analysis results are presented. However, the table's format is not very clear. I strongly recommend revising the tables. Abbreviations should definitely be added with their full names below the tables. This article's format presents an image that will be overwhelming for the reader.

There's another shortcoming in the presentation of the results. This section lists the relevant clinical pathology and ECG differences between the groups. However, no reason is given. The presentation of the results appears confusing. This may be due to the sheer number of results presented. However, I must point out that the article, in its current form, appears very confusing and doesn't provide a clear flow for the reader.

Placing the headings of Table 3 in the row on the left instead of the column above may make the article more understandable for the reader.

- Discussion

The study should explain the relationship between DM and changes detectable on a single-lead ECG. This pathophysiological explanation needs to be detailed. I believe the existing explanations are inadequate. Reading the study in this way will raise many doubts in the reader.

Overall, the article is very well designed, but I think the writing and presentation of the results are not very good.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 116115

Title: Discriminating Diabetes Mellitus from Single-Lead ECG Using Machine Learning and Multinomial Regression

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08588323
Position: Peer Reviewer
Academic degree and professional title: PhD, Postdoc
Reviewer's Country/Territory: China
Author's Country/Territory: Russia

Manuscript submission date: 2025-11-02

Reviewer chosen by: Meng-Liu Luo

Reviewer accepted review: 2025-12-12 02:27

Reviewer performed review: 2025-12-12 07:34

Review time: 5 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **No** Do authors' affiliations correspond to the content of the manuscript? **Yes** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes** Are the Key Words complete? **Yes**

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Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
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Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The authors have addressed several structural and presentation-related issues in the revised manuscript, including consolidation of inclusion and exclusion criteria, addition of methodological subheadings, clarification of the timing of ECG acquisition, and moderation of statements related to “early screening.” These changes have improved the overall readability and internal consistency of the manuscript. The research topic remains of interest and has potential clinical value, particularly in the context of combining wearable single-lead ECG technology with machine-learning approaches for diabetes identification.

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However, from the perspective of methodological rigor and interpretability of the results, the current revision does not yet adequately resolve several key concerns. These issues directly affect the reliability of model training labels, the representativeness of the study population, and the independence of the association between ECG features and diabetes status. Without further clarification or additional analyses, the manuscript is not yet suitable for acceptance.

1. Diagnostic and classification criteria for diabetes mellitus remain insufficiently defined

Although the revised manuscript provides additional information on glucose measurement, the diagnosis and classification of diabetes mellitus still rely primarily on capillary glucose thresholds combined with medical history and treatment information. It remains unclear whether internationally accepted standards (e.g., ADA or WHO criteria) were followed, and no systematic description is provided regarding the use of HbA1c, OGTT, C-peptide, or autoantibody testing for subtype classification. This approach may introduce label noise and misclassification, thereby directly affecting the reliability of machine-learning model training and validation.

It is recommended that the Methods section clearly specify the diagnostic and classification guidelines used and the biochemical criteria applied. If standardized diagnostic or classification criteria were not consistently implemented or cannot be supplemented, the resulting classification bias should be explicitly acknowledged and discussed in the Limitations.

2. Enrollment strategy and potential selection bias remain unclear

The revised manuscript does not clearly state whether participants were enrolled consecutively during the study period or selected based on data completeness and signal quality. In addition, no information is provided regarding the numbers and reasons for exclusion at each stage of screening, inclusion, and analysis. The absence of this information prevents assessment of sample representativeness and the direction of

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potential selection bias.

It is recommended that the authors clarify in the Methods whether enrollment was consecutive and specify the clinical settings from which participants were recruited. A flow diagram detailing screening, inclusion, and exclusion (with corresponding numbers and reasons) should be provided. If feasible, a comparison of baseline characteristics between included and excluded participants (as supplementary material) would further help assess selection bias. If these additions are not possible, the limited representativeness of the study population should be explicitly stated in the Limitations.

3. Insufficient control of ECG-related confounding factors

The current exclusion criteria address only pronounced QRS morphology abnormalities and signal quality issues, but do not systematically account for cardiac comorbidities (such as ischemic heart disease, cardiomyopathies, or arrhythmias) or medications known to affect ECG features, particularly the QT interval. As a result, part of the model's discriminative signal may reflect underlying cardiovascular comorbidity rather than diabetes itself.

It is recommended that the authors clarify whether major cardiac comorbidities and QT-modifying medications were recorded and either excluded or adjusted for in the analysis. Where possible, key conditions (e.g., coronary artery disease, heart failure, atrial fibrillation) should be included as covariates or explored through stratified or sensitivity analyses. If data limitations preclude such analyses, this confounding risk should be clearly acknowledged, and causal interpretations of diabetes-specific ECG signatures should be appropriately tempered.

4. Study positioning requires further refinement

Although the authors have clarified that ECG recordings were obtained after diabetes diagnosis, some statements may still be interpreted as suggesting an early screening application. Given the data source and current model performance, a more appropriate

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positioning would be as an adjunctive identification or risk-enrichment tool rather than an independent screening or classification method.

It is recommended that wording in the Abstract and Discussion be further harmonized to emphasize the model's role in supporting identification or prompting confirmatory biochemical testing, while avoiding language that could be construed as replacing standard diagnostic approaches or enabling population-level early screening.

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Reviewer's code: 08478544

Position: Peer Reviewer

Academic degree and professional title: Academic Fellow, Assistant Professor, Clinical Assistant Professor (Honorary), MD

Reviewer's Country/Territory: Türkiye

Author's Country/Territory: Russia

Manuscript submission date: 2025-11-02

Reviewer chosen by: Meng-Liu Luo

Reviewer accepted review: 2025-12-12 05:18

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Review time: 9 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **No** Do authors' affiliations correspond to the content of the manuscript? **Yes** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes**

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Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The authors made all of my revisions, so I thinsk the article is acceptable now.