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Metabolic Age and Phase Angle in Iranian Population: How Is Their Health Status?

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1 Original submission

2 comments · 1 Jun 2025 – 28 Jun 2025

Referee 1 Reviewer

MAJOR REVISION 1 Jun 2025

The research article evaluates the health status of the Iranian population by investigating metabolic age (MA) and phase angle (PA) as indicators of fitness and health. There are some issues regarding the manuscript.
Methods:
1. Convenience Sampling: The use of convenience sampling limits the generalizability of the findings. A discussion of the potential biases introduced by this sampling method is needed.
2. Inclusion Criteria: The inclusion criteria of "healthy status without apparent diseases" are vague. Clearer, more objective criteria are needed to define "healthy."
3. Missing Information: It is important to describe how "healthy status" was determined. Was it based on self-report, medical records, or specific clinical assessments?
4. Confounder Control: While the study mentions excluding potential confounders, it does not specify which confounders were considered and how they were controlled.
5. Data Analysis Details: More details on the statistical analyses are needed. For example, were the data normally distributed? If not, were non-parametric tests considered?
Results:
6. Correlation vs. Causation: The manuscript should emphasize that correlation does not equal causation, especially when interpreting the relationships between age, MA, and PA.

Tables and Figures:
7. Figure 1: Figure 1 is a pie chart showing gender distribution. This is basic information, and its utility could be questioned.

Referee 2 Reviewer

MINOR REVISION 28 Jun 2025

Dear AE,
Thank you very much for giving me this opportunity to review this manuscript.

This manuscript investigates metabolic age (MA) and phase angle (PA) as biomarkers for health status in a healthy Iranian population (*n=445*). Key findings include a strong correlation between MA and chronological age (*r=0.652, p<0.05*) and a sex-based difference in PA (higher in males, p<0.05). The study leverages bioelectrical impedance analysis (BIA) and proposes PA as a prognostic marker for health interventions. Strengths include a robust sample size and clear methodology, but limitations include the cross-sectional design and lack of longitudinal data.

In-Depth Review
Methodology & Results
1. Sample: Convenience sampling from a Tehran clinic may limit generalizability. No justification for excluding confounders (e.g., subclinical conditions) is provided.
2. MA & Age Correlation: Strong linear relationship (*MA = 9.375 + 0.738[age]*), suggesting lifestyle impacts metabolic health.
3. Sex Differences: PA was higher in males (*6.78±0.69 vs. 6.18±1.27, p<0.05*), likely reflecting muscle mass differences. MA did not differ by sex (p>0.05).

4. PA Prognostic Value: Weak negative correlation between PA and MA (*r=-0.103, p=0.031*), aligning with literature on cell membrane integrity.

Concerns:
5. BIA Limitations: No discussion of potential errors (e.g., hydration status affecting PA).
6. Clinical Utility: MA's predictive power for health outcomes (e.g., NCD risk) is not explored.

Discussion
7. No comparison to Iranian PA reference values (cf. Barbosa-Silva et al., 2005).
8. MA's clinical relevance (e.g., actionable thresholds) is underexplored.

9. Were participants fasting, and was their hydration status controlled during BIA?
10. How might MA/PA integrate into existing health screening protocols in Iran?

Overall, the study provides valuable insights into MA/PA as health biomarkers but requires clarifications on methodology and clinical applicability.

Final Decision: Minor Revision

Kind Regards | Publisher Supervisor

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewer 1:

- Comment - Convenience Sampling:

Response: Thank you for this valuable point. Specifically, we note that although participants were recruited from a central preventive clinic in Tehran, this may not fully reflect the broader Iranian population, and results should be interpreted accordingly.

- Comment - Inclusion Criteria:

Response: We appreciate the suggestion. The Methods section now clarifies that “healthy status” was defined as individuals without a known history of chronic or acute disease, as assessed through clinical interview and examination during the routine check-up at the health promotion clinic. This includes absence of diagnosed cardiovascular, metabolic, infectious, or autoimmune conditions.

- Comment - Missing Information on Health Determination:

Response: As noted above, the assessment was conducted via standardized clinical interviews and physical examination, as part of the routine evaluation at the clinic.

- Comment - Confounder Control:

Response: We thank the reviewer for this insight. In the Methods section, we now specify that individuals with any acute or chronic condition, as well as those under medication that could influence body composition (e.g., corticosteroids), were excluded to minimize confounding. This was done prior to data collection.

- Comment - Data Analysis Details:

Response: We appreciate this suggestion. A normality test was conducted for continuous variables. The variables were approximately normally distributed, justifying the use of parametric tests.

- Comment - Correlation vs. Causation:

Response: Thank you for highlighting this. In the Discussion section (paragraph 5), we have now emphasized that due to the cross-sectional design, we can only report associations, not causal relationships.

- Comment - Figure 1 - Pie Chart of Gender:

Response: We understand the concern. Figure 1 has now been removed to streamline the presentation. The gender distribution is still reported in Table 1 and the text.

Reviewer 2:

- Comment - Sample and Confounders:

Response: We agree and now clearly explain in the Methods section that participants underwent a health screening visit including history and physical exam to exclude both apparent and subclinical conditions that could influence outcomes.

- Comment - MA & Age Correlation:

Response: We thank the reviewer. We have reinforced this point in the Discussion, noting that the strong correlation may indicate accelerated biological aging due to lifestyle factors, and it can be used for health education purposes.

- Comment - Sex Differences in PA:

Response: This interpretation is valid and now explicitly mentioned in the Discussion section. We reference literature that supports muscle mass as a determinant of PA and emphasize that this could partly explain the observed sex differences.

- Comment - PA Prognostic Value:

Response: We have expanded the Discussion to link our findings with previous studies on PA as an indicator of cell integrity and aging, supporting its potential prognostic value.

- Comment - BIA Limitations:

Response: We appreciate this. We have now added a paragraph in the Discussion regarding limitations of BIA, particularly its sensitivity to hydration status, recent food intake, and electrode placement.

- Comment - Clinical Utility of MA:

Response: This is a crucial point. While our current data are cross-sectional, we have added a sentence in the Discussion suggesting future longitudinal studies to evaluate the predictive value of MA for metabolic syndrome or cardiovascular events.

- Comment - No Comparison to Iranian PA Reference Values:

Response: We now discuss Barbosa-Silva's reference values in the Discussion, noting that the Iranian population in our study exhibited lower average PA, suggesting potential baseline differences in lifestyle or nutrition.

- Comment - MA’s Clinical Relevance:

Response: While there is no standardized MA threshold yet, we now state in the Discussion that individual MA higher than chronological age may signal reduced metabolic fitness and merit intervention.

- Comment - Fasting/Hydration During BIA:

Response: Yes, all participants underwent BIA in the morning after an overnight fast and were advised to avoid strenuous activity the day before. This procedural detail has been added to the Methods section.

- Comment - Integration into Screening Protocols:

Response: An excellent point. In the Discussion, we propose that MA/PA assessment can complement routine health checks, particularly in preventive clinics and health promotion centers, offering non-invasive early warning markers.

2 Revision 1

1 comment · 16 Aug 2025

Editor-in-Chief

ACCEPT 16 Aug 2025

Manuscript ID: 162002
Dear Dr. Abbas Nurmohammadi
Thank you for submitting your manuscript to Annals of Military and Health Sciences Research. We appreciate the opportunity to consider your work for publication.
After careful evaluation and peer review, we are pleased to inform you that your manuscript has been assessed as suitable for publication.
Best regards,

Dr. Mohsen Chamanara
Editor-in-Chief
Annals of Military and Health Sciences Research