

## Responses to Reviewers

We thank the Reviewers for their thoughtful comments. Here our responses to the points that were raised in their review.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an important paper about one of the most devastating complications of diabetes. Please update the paper based on the following suggestions.

1. Please include recommendations for omega 3 for adults where you are explaining effects of supplementation on wound healing. Did participants in the reference 28 receive 1000 mg or 2000 mg of omega 3 daily? please make it clear. Also Please report the sample size for this study.

**Author's reply: We have included suggestion about the dose and schedule recommended for Omega 3. We have specified that participants in the reference 28 received 2000 mg of Omega 3 daily. Sample size of study 28 has been reported and added in the main text and table.**

2. In the last paragraph of omega 3, it looks like you are talking about one study but there are two different references 28 and 29. please make it clearer.

**Author's reply: We had clarified the last paragraph on omega 3, reference 29 was related to the comment on the study (28) by Moore et Al.**

3. Did reference 34 had zero patient in the study? Please correct it.

**Author's reply: reference 34 included 60 patients. We have corrected the mistake in the main text.**

4. please report decrease in HbA1c and sample size for reference 34.

**Author's reply: Decresae in HbA1 was  $-0.6 \pm 0.5$  vs.  $-0.2 \pm 0.4\%$ . We added the information required.**

5. please substitute UI with IU for vitamin D.

**Author's reply: UI has been replaced with IU.**

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Non-healing diabetic foot ulcers (DFU) are the most significant and devastating complications of diabetes mellitus. More than 25% of nonhealing DFU can ultimately lead to amputation of the lower extremity within 6–18 months after the first manifestation of the wound. Although wound healing is complex, nutritional status is crucial in soft tissue repair. Malnutrition is highly prevalent and overlooked in patients with diabetes and chronic wounds. Moreover, to date, we do not have clear recommendations or evidence about the use of nutritional supplements for improving wound healing in patients with DFU. This article aimed to evaluate the current evidence on the use of nutritional supplementation in wound healing in patients with DFU. The author briefly analyzed the current evidence on the use of nutritional supplements of proteins or amino acids, fatty acids, probiotics, vitamins, and trace elements in the wound healing process in patients with DFU. Core Tip Malnutrition is common in patients with diabetes and chronic wounds. To date, we do not have clear recommendations or evidence about the use of nutritional supplements for improving wound healing in patients with DFU. This article aimed to evaluate the current evidence on the use of nutritional supplementation in wound healing in patients with DFU. In General: it's a good paper and the subject of the manuscript is applicable and useful. Title: the title properly explains the purpose and objective of the article Abstract: abstract contains an appropriate summary for the article, the language used in the abstract is easy to read and understand, and there are no suggestions for improvement. Introduction: authors do provide adequate background on the topic and reason for this article and describe what the authors hoped to achieve. Results: the results are presented clearly, the authors provide accurate research results, and there is sufficient evidence for each result. Conclusion: in general: Good and the research provides sample data for the authors to make their conclusion.

**Author's reply: Thank You**

Grammar: Need Some revision. (Check The Paper Comments).

**Author's reply: We have revised the grammar following the kind suggestions in comments.**

Please provide the following information in the Paper 1. Conflict of Interest 2. Source of Funding

**Author's reply: The information's required have been provided**

Finally, this was an appealing article, in its current state it adds much new insightful information to the field.

**Author's reply: Thank you**

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: What does the authors mean by "It is known that malnutrition delays the inflammatory phase of the healing process," - is it prolongation of inflammatory phase or delay? Delay means the wound will arrest in hemostasis phase?

**Author's reply: Thank you for the observation. We agree with the reviewer: the word delay is improper. We mean that poor nutritional status is associated with impaired inflammatory response in wound healing process. So, we have replaced the word "delay" with "impair" hoping that this change makes the sentence clearer.**

Please check for DFU vs DFUs we included in this analysis- the authors have not done any analysis; this manuscript is summary of published literature role they play in the healing process of wounds is still largely unknown and there is growing interest in understanding their specific effects on the cellular / molecular factors involved- the role of resolvins have studies for long and multiple published (PMID: 33793355) articles have shown positive results.

**Author's reply: We have been invited by editorial board to write a minireview on the topic "nutritional supplement and wound healing in patient with diabetic foot ulcer". In this form of paper analysis of original data is not possible. We are really thankful and kindly accept the suggestion of a mention about the role of resolvins on wound healing including 1 more reference (ref 16 ).**

Please check and modify the statement few studies that have evaluated the effects of omega-3 fatty acids from fish oil - please list some studies

**Author's reply: Thank you for the correct suggestions. We have included three more studies (ref 24-25-26)**

Please include a Table listing all studies, the nutrient being used, patient population, nutrient dose, and the outcome of the study.

**Author's reply: Table 1 list all RCT included in the paper with information required about the nutrient used, population, nutrient dose, and the outcomes.**

Please check the manuscript thoroughly for the English language. For examples only proper nouns should be capitalized in between sentence

**Author's reply: We have revised the grammar and English language was certified again by an external native speaking editor.**

Round 2:

The authors need to include Table 1 in the manuscript or in the files.

**Specific Comments To Authors:** In response to reviewers' comments, the author mentioned that RCTs have been listed and included in the manuscript but there is no table, please include.

**Author's reply:** We add the table.