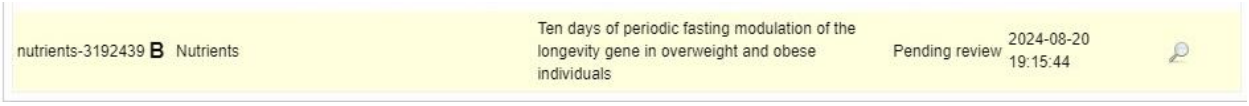
BUKTI KORESPONDENSI

ARTIKEL JURNAL INTERNASIONAL BEREPUTASI SCOPUS Q1

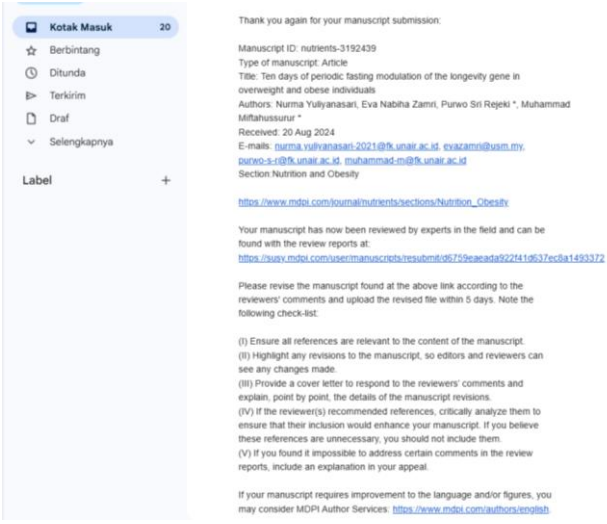
Judul Artikel	: The Impact of Ten Days of Periodic Fasting on the Modulation of the Longevity Gene in Overweight and Obese Individuals: A Quasi-Experimental Study
Jurnal	**:** Nutrients
Penulis	**:** Nurma Yuliyanasari, Eva Nabiha Zamri, Purwo Sri Rejeki, and Muhammad Miftahussurur

NO	PERIHAL	TANGAL
1	Bukti Submit artikel	20 Agustus 2024
2	Bukti revisi minor	30 Agustus 2024
3	Bukti revisi dan resubmit artikel setelah revisi	11 September 2024
4	Bukti konfirmasi artikel accepted	12 September 2024
5	Payment confirmation	14 September 2024
6	Bukti konfirmasi artikel published online	15 September 2024

1. Bukti submit artikel dan invoice pembayaran



2. Bukti revisi minor



3. Bukti revisi dan resubmit artikel setelah revisi

a. Bukti email

Thank you very much for providing the revised version of your paper:

Manuscript ID: nutrients-3192439
Type of manuscript: Article
Title: Ten days of periodic fasting modulation of the longevity gene in overweight and obese individuals
Authors: Nurma Yuliyanasari, Eva Nabiha Zamri, Purwo Sri Rejeki *, Muhammad Miftahussurur *
Received: 20 Aug 2024
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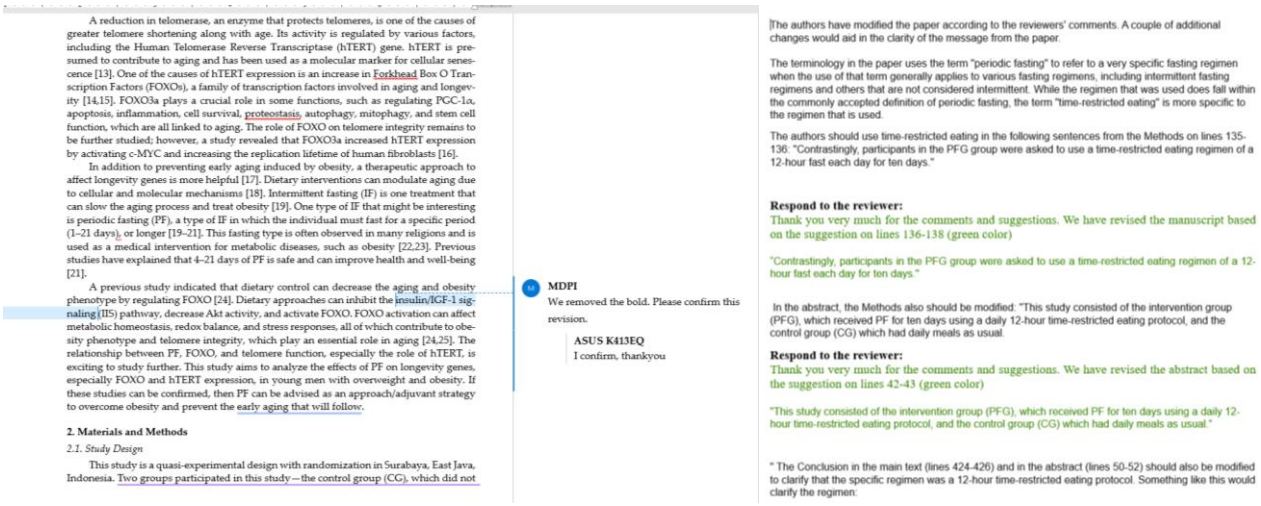

A reduction in telomerase, an enzyme that protects telomeres, is one of the causes of greater telomere shortening along with age. Its activity is regulated by various factors, including the Human Telomerase Reverse Transcriptase (hTERT) gene. hTERT is presumed to contribute to aging and has been used as a molecular marker for cellular senescence [13]. One of the causes of hTERT expression is an increase in Forkhead Box O Transcription Factors (FOXOs), a family of transcription factors involved in aging and longevity [14,15]. FOXO3a plays a crucial role in some functions, such as regulating PGC-1α, apoptosis, inflammation, cell survival, proteostasis, autophagy, mitophagy, and stem cell function, which are all linked to aging. The role of FOXO on telomere integrity remains to be further studied; however, a study revealed that FOXO3a increased hTERT expression by activating c-MYC and increasing the replication lifetime of human fibroblasts [16].

In addition to preventing early aging induced by obesity, a therapeutic approach to affect longevity genes is more helpful [17]. Dietary interventions can modulate aging due to cellular and molecular mechanisms [18]. Intermittent fasting (IF) is one treatment that can slow the aging process and treat obesity [19]. One type of IF that might be interesting is periodic fasting (PF), a type of IF in which the individual must fast for a specific period (1–21 days), or longer [19–21]. This fasting type is often observed in many religions and is used as a medical intervention for metabolic diseases, such as obesity [22,23]. Previous studies have explained that 4–21 days of PF is safe and can improve health and well-being [21].

A previous study indicated that dietary control can decrease the aging and obesity phenotype by regulating FOXO [24]. Dietary approaches can inhibit the insulin/IGF-1 signaling (IIS) pathway, decrease Akt activity, and activate FOXO. FOXO activation can affect metabolic homeostasis, redox balance, and stress responses, all of which contribute to obesity phenotype and telomere integrity, which play an essential role in aging [24,25]. The relationship between PF, FOXO, and telomere function, especially the role of hTERT, is exciting to study further. This study aims to analyze the effects of PF on longevity genes, especially FOXO and hTERT expression, in young men with overweight and obesity. If these studies can be confirmed, then PF can be advised as an approach/adjuvant strategy to overcome obesity and prevent the early aging that will follow.

2. Materials and Methods

2.1. Study Design

This study is a quasi-experimental design with randomization in Surabaya, East Java, Indonesia. Two groups participated in this study—the control group (CG), which did not

MDPI
We removed the bold. Please confirm this revision.

ASUS K413EQ
I confirm, thankyou

The authors have modified the paper according to the reviewers' comments. A couple of additional changes would aid in the clarity of the message from the paper.

The terminology in the paper uses the term "periodic fasting" to refer to a very specific fasting regimen when the use of that term generally applies to various fasting regimens, including intermittent fasting regimens and others that are not considered intermittent. While the regimen that was used does fall within the commonly accepted definition of periodic fasting, the term "time-restricted eating" is more specific to the regimen that is used.

The authors should use time-restricted eating in the following sentences from the Methods on lines 135-136: "Contrastingly, participants in the PFG group were asked to use a time-restricted eating regimen of a 12-hour fast each day for ten days."

Respond to the reviewer:
Thank you very much for the comments and suggestions. We have revised the manuscript based on the suggestion on lines 136-138 (green color)

"Contrastingly, participants in the PFG group were asked to use a time-restricted eating regimen of a 12-hour fast each day for ten days."

In the abstract, the Methods also should be modified: "This study consisted of the intervention group (PFG), which received PF for ten days using a daily 12-hour time-restricted eating protocol, and the control group (CG) which had daily meals as usual.

Respond to the reviewer:
Thank you very much for the comments and suggestions. We have revised the abstract based on the suggestion on lines 42-43 (green color)

"This study consisted of the intervention group (PFG), which received PF for ten days using a daily 12-hour time-restricted eating protocol, and the control group (CG) which had daily meals as usual."

" The Conclusion in the main text (lines 424-426) and in the abstract (lines 50-52) should also be modified to clarify that the specific regimen was a 12-hour time-restricted eating protocol. Something like this would clarify the regimen:

4. Bukti konfirmasi artikel accepted

Congratulations on the acceptance of your manuscript, and thank you for submitting your work to Nutrients:

Manuscript ID: nutrients-3192439
Type of manuscript: Article
Title: Ten days of periodic fasting modulation of the longevity gene in overweight and obese individuals
Authors: Nurma Yuliyanasari, Eva Nabiha Zamri, Purwo Sri Rejeki *, Muhammad Miftahussurur *
Received: 20 Aug 2024
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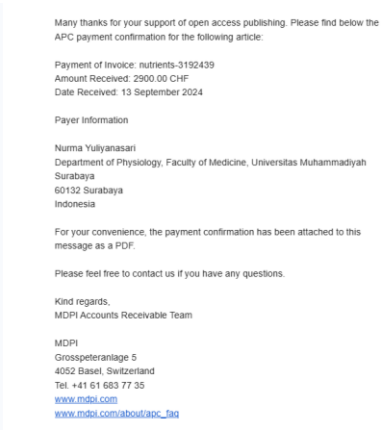

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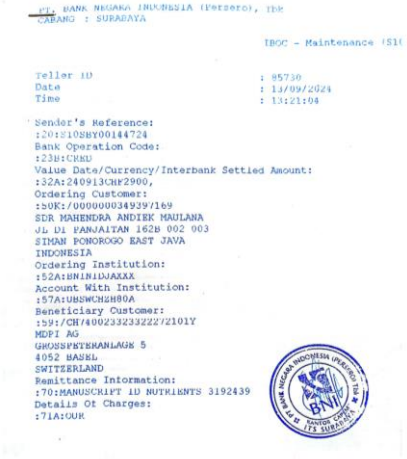

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6. Bukti konfirmasi artikel published online

[Nutrients] Manuscript ID: nutrients-3192439; doi: 10.3390/nu16183112. Paper has been published. Eksternal Kotak Masuk ×

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Min, 15 Sep 2024, 17.30

Terjemahkan ke Indonesia

Dear Authors,

We are pleased to inform you that your article "The Impact of Ten Days of Periodic Fasting on the Modulation of the Longevity Gene in Overweight and Obese Individuals: A Quasi-Experimental Study" has been published in Nutrients and is available online at the following links:

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Article

The Impact of Ten Days of Periodic Fasting on the Modulation of the Longevity Gene in Overweight and Obese Individuals: A Quasi-Experimental Study

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Abstract: Background: Fasting potentially alters the aging process induced by obesity by regulating telomere integrity, which is related to longevity genes. However, the impact of periodic fasting (PF) on the expression of longevity genes, particularly Forkhead Box O Transcription Factors (FOXO3a) and the Human Telomerase Reverse Transcriptase (hTERT), is not fully understood. This study aimed to analyze the effects of PF, specifically on FOXO3a, hTERT expression, and other associated factors. Methods: A quasi-experimental 10-day study was conducted in Surabaya, East Java, Indonesia. This study consisted of an intervention group (PFG), which carried out PF for ten days using a daily 12 h time-restricted eating protocol, and a control group (CG), which had daily meals as usual. FOXO3a and hTERT expression were analyzed by quantitative real-time qPCR. A paired *t*-test/Wilcoxon test, independent *t*-test/Mann–Whitney U-test, and Spearman's correlation test were used for statistical analysis. Result: Thirty-six young men participated in this study. During the post-test period, FOXO3a expression in the PFG increased 28.56 (±114.05) times compared to the pre-test, but the difference was not significant. hTERT expression was significantly higher in both the CG and PFG. The hTERT expression in the PFG was 10.26 (±8.46) times higher than in the CG, which was only 4.73 (±4.81) times higher. There was also a positive relationship between FOXO and hTERT in the CG. Conclusions: PF significantly increased hTERT expression in the PFG; however, no significant increase was found in FOXO3a expression. PF regimens using the 12 h time-restricted eating approach may become a potential strategy for preventing obesity-induced premature aging by regulating longevity gene expression.

Keywords: FOXO; h-TERT; obesity; periodic fasting; telomerase