Dietary Inflammatory Index is associated with Healthy Eating Index, Alternative Healthy Eating Index, and dietary patterns among Iranian adults

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Abstract

Background: Recent investigations have evaluated the effect of the inflammatory potential of diet in several populations by calculating the Dietary Inflammatory Index (DII) score. We aimed to evaluate the association of the DII with the Healthy Eating Index (HEI), the Alternative Healthy Eating Index (AHEI), and dietary pattern (DP) among healthy Iranian adults.

Methods: A cross-sectional study was conducted among 4365 middle-aged adults. Major DPs and DII score were identified using a validated semi-quantitative food frequency questionnaire (FFQ). Poisson regression was used to evaluate the association of DPs, HEI, and AHEI across tertiles of DII.

Results: After adjustment for confounding variables, a low HEI (HEI < 55) and AHEI (AHEI < 56.5) were more prevalent among the participants in the highest tertile of DII compared to the first tertile (PR: 1.13, P-value <.05; PR: 1.10, P-value <.05; respectively). Adherence to a balanced healthy dietary pattern was significantly lower in subjects with a diet that was more pro-inflammatory compared to those with anti-inflammatory diet (PR: 0.85, P-value P <.01). No significant association was found between the DII and a western DP. High levels of HDL and hip and waist circumference were observed in the highest tertile of DII, and high levels of dietary intake of protein and fiber, minerals, fasting blood glucose, and monounsaturated fat were reported in the lowest tertile of DII.
An unhealthy diet has a considerable impact on inflammatory status\(^1\) and can thereby increase the risk of chronic non-communicable diseases, such as cardiovascular disease (CVD), diabetes mellitus, and cancer.\(^2\) Dietary Inflammatory Index (DII\(^8\)) has been designed to quantify the inflammatory potential of a diet.\(^6\)\(^7\) The DII score is calculated based on 45 food parameters that are included in an individual's dietary pattern (DP).\(^7\)

A DP can be described as a combination of food items consumed frequently\(^9\) that differs among populations with various sex, races, and cultures.\(^8\) Western DP is considered to be a relatively unhealthy DP characterized by high intake of foods like butter, red meat, processed meat, refined grains, eggs, potatoes, and sugared-sweetened beverages; it is known to enhance the serum concentrations of some inflammatory markers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)).\(^9\)\(^11\) A decreased inflammatory state was reported in those with Mediterranean DP defined as a healthy pattern, which is characterized by high consumption of foods like olive oil, vegetables, fruits, and fish.\(^11\)

Besides the DII, two other indices are used to show diet quality and effectiveness of diet called Healthy Eating Index (HEI) and Alternative Healthy Eating Index (AHEI).\(^12\) Schwingshackl et al\(^12\) demonstrated that diets with high HEI and AHEI scores are associated with higher public health status; and Barbaresko et al\(^13\) showed that healthy diets reduce inflammation. However, the association between the DII with major DPs, HEI, and AHEI has not been evaluated. We hypothesized that a higher DII would be correlated with lower HEI, lower AHEI, lower adherence to healthy DP, and higher adherence to unhealthy DP.

2 | MATERIALS AND METHODS

2.1 | Study population

In the current study, data obtained as part of the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study participants were used. This study is a prospective study of 9761 adults (35–65 years at baseline) from Iran (Mashhad), which was started at 2010 and designed to evaluate various cardiovascular disease risk factors.\(^14\) Exclusion criteria were as follows: (a) participants who had energy intake of <800 or >4200 kilocalorie and (b) participants who filled less than 90 percent of the food frequency questionnaire (FFQ) items. Therefore, the rest of the study population (n = 4365) were included in this study. The Human Research Ethics Committee of Mashhad University of Medical Sciences (MUMS) approved the study procedure and consent form. All the participants of the study provided informed written consent.

2.2 | Dietary pattern assessment

Two major DPs were identified by Asadi et al in Iranian adults of Mashhad study.\(^15\): balanced DP and western DP. A validated semi-quantitative FFQ that was completed by an experienced nutritionists was utilized to determine the main DPs of the population study.\(^16\) Several frequency groups (never, rarely, per month, per week, and per day) were included in the questionnaire for each food item and portion size. To derive DPs according to the 22 food items of the FFQ, factor analysis was used.\(^15\) Varimax rotation of the factors was performed for a better interpretation. An eigenvalue >1 of the components, the scree plot, and the interpretability of the factors were considered for identifying the number of factors.\(^15\) Finally, a score was determined for each individual in both of identified DPs. The percentage variance explained by each factor was not considered, since this criterion largely depends on the whole number of variables included in the analysis.\(^17\)

2.3 | Dietary Inflammatory Index

The DII score development and validation were described previously by Asadi et al.\(^18\) DII was calculated based on 28 food parameters in the present analysis. The DII score is globally ranged from a minimum of −8.87 (the most anti-inflammatory diet) to a maximum of +7.98 (the most pro-inflammatory diet).\(^7\) We categorized the DII score into tertiles, defined as T1, T2, and T3. T1 was the most anti-inflammatory tertile, and T3 was the most pro-inflammatory tertile (T1: <-0.02; T2: ≥-0.02 and < 1.18; T3: ≥1.18).

2.4 | Healthy eating index assessment

Development and validation of HEI were described by Basiotis et al at 2005\(^19\) at first time and were completed by Guenther et al at
2010 (HEI-2010). HEI-2010 has 12 components: 9 adequacy and 3 moderation components. The complete score is 100, and the higher scores describe higher quality of individual's diet. HEI was calculated based on FFQ.

### 2.5 Alternative Healthy Eating Index assessment

Assessing of AHEI was described by Chiuve et al. This index predicts the association chronic disease risk and diet that shows inverse association between them. AHEI-2010 is scored in the range of 0 (non-adherence) to 110 (perfect adherence) based on components. Each component has been scored in this range: 0-10 (worst to best). AHEI was calculated based on FFQ too.

### 2.6 Assessment of other variables

Anthropometric criteria, laboratory tests, blood pressure (BP), physical activity level (PAL), and demographic and socioeconomic characteristics were measured in all subjects of the study according to previous study.

### 2.7 Statistical analysis

Statistical analysis was performed using SPSS version 16.0 (SPSS, Chicago, IL). Descriptive analysis was used across tertiles of DII to compare the main variables of interest (demographic and lifestyle, physical measurements, and lipid and metabolic markers) among the study population. To report the differences of quantitative and qualitative data in various DII tertiles, analysis of variance (ANOVA) and chi-squared tests were used, respectively. Poisson regression models were used to analyze the correlation of DPs, HEI, and AHEI with DII tertiles, using the first tertile as the reference group. Multiple Poisson regression model was adjusted for sex, age, PAL, smoking status, marriage, education level, BMI, WC, diabet drug, lipid-lowering drug, and antihypertensive drug use. The prevalence ratio (PR) with 95% confidence interval (CI) was used to report the association of DPs, HEI, and AHEI across tertiles of DII.

### 3 RESULTS

Final analysis was undertaken in a sample of 4365 participants of the MASHAD study after exclusions. We divided all participants into tertiles based on DII score (T1: <-0.02; T2: 0.02 and < 1.18; T3: ≥1.18).

The baseline characteristics of the study population across DII tertiles are shown in Table 1. Participants in the highest tertile of DII were more likely to be female and older compared to those in the lowest tertile. They also had the highest PAL and %BF (body fat percentile) and the lowest fasting blood glucose (FBG). On the other hand, subjects in the first tertile were more likely to be married, have diabetes mellitus, and to use anti-diabetic drugs more than the two other tertiles. They also had the highest mid-upper arm circumference (MAC) and the lowest high-density lipoprotein cholesterol (HDL-C). We also found that subjects in the second tertile had the lowest body mass index (BMI), hip circumference (HC), waist circumference (WC), and waist-to-height ratio (WHtR) and, also, used anti-hypertensive drugs and lipid-lowering drugs more than those in the first and last DII groups.

As shown in Table 2, the dietary intake of protein, dietary fiber, iron, magnesium, zinc, vitamin C, and carotene was higher among subjects who consumed the most anti-inflammatory diet, while participants in the third tertile had lower intake of energy, monounsaturated fat, and copper.

The association between HEI, AHEI, balanced DP, and western DP in different tertiles of DII score using three different models for adjustment is shown in Table 3. After adjusting for all confounding factors, the PR of lower HEI (HEI < 55) was found to be higher among those with higher DII, while adherence to a balanced DP was more prevalent among participants with lower DII score. In addition, the highest tertile of DII was associated with lower AHEI (AHEI < 56.5) prevalent.

### 4 DISCUSSION

We aimed to evaluate the relationship between DII, HEI, AHEI, and DP in a healthy population of Iranian adults. Subjects with lower HEI and AHEI had a more pro-inflammatory diet, whereas adherence to balanced DP was more prevalent among those with an anti-inflammatory diet.

Dietary Inflammatory Index is a scoring system developed by Shivappa et al, which is used to assess the anti-inflammatory and pro-inflammatory content of the diet. A high DII has been shown to be associated with metabolic syndrome, which would increase CVD risk. A large body of evidence suggests that DP may play a substantial role in the development of various chronic diseases including CVD and diabetes. Healthy DPs, which are known to decrease inflammation, are characterized by limited consumption of red and processed meat, high intake of vegetables, fruits, whole grains, sea food, and low-fat milk products. The effect of two different DPs, balanced and western pattern, on DII score was evaluated in this study in Iranian population. According to our results, a balanced pattern is associated with a lower DII score as this pattern is a rich source of dietary fiber.

The possible relation of DII and DP in different medical conditions has been proposed. Sharma et al have demonstrated that DII does not affect overall mortality or combined mortality, recurrence, or metastasis colorectal cancer patients. However, there was reverse association between DII and relapse-free survival as well as alternate Mediterranean diet score (MDS). They have also proposed that decrease in DII was correlated with a higher amount of plant-based food intake. In the settings of chronic disease, the DII is
### TABLE 1 Characteristics of participants according to the tertiles of Dietary Inflammatory Index

| Variables                        | Dietary Inflammatory Index |        |        |        |
|----------------------------------|-----------------------------|--------|--------|--------|
|                                  | T1 (n = 1434)               | T2 (n = 1442) | T3 (n = 1489) |
| **Demographic and lifestyle**    |                             |        |        |        |
| Age (years)                      | 49.02 ± 7.84a               | 48.80 ± 7.98a | 49.60 ± 7.83b |
| Sex, % (n)                       |                             |        |        |        |
| Male                             | 44.70 (641)a                 | 44.60 (643)b | 38.10 (567)b |
| Female                           | 55.30 (793)a                 | 55.40 (799)a | 61.90 (922)b |
| **Marital status, % (n)**        |                             |        |        |        |
| Single/divorced/widow            | 5.60 (80)a                   | 7.60 (109)b | 8.10 (121)c |
| Married                          | 94.40 (1354)a                | 92.40 (1333)b | 91.90 (1368)c |
| **Education, % (n)**             |                             |        |        |        |
| Low (trade school)               | 53.30 (761)                  | 54.30 (781) | 54.90 (815) |
| Moderate (high school)           | 38.40 (548)                  | 37.90 (545) | 38.70 (575) |
| High (university)                | 8.30 (119)                   | 7.90 (113) | 6.30 (94) |
| **Smoking status, % (n)**        |                             |        |        |        |
| Non smoker                       | 67.60 (970)                  | 68.80 (992) | 70.70 (1053) |
| Ex- smoker                       | 10.80 (155)                  | 10.50 (151) | 9.30 (139) |
| Current smoker                   | 21.50 (309)                  | 20.70 (299) | 19.90 (297) |
| **Physical activity level**      | 1.56 ± 0.28a                 | 1.59 ± 0.28b | 1.60 ± 0.27b |
| **Diagnosed diseases, % (n)**    |                             |        |        |        |
| Diabetes                         | 10.90 (157)a                 | 9.60 (139)a | 6.90 (102)b |
| Hypertension                     | 12.80 (183)                  | 11.30 (163) | 11.50 (171) |
| Dyslipidemia                     | 88.60 (1270)                 | 87.30 (1259) | 87.50 (1303) |
| **Use of medication, % (n)**    |                             |        |        |        |
| Anti-diabetic drug               | 2.70 (39)a                   | 1.90 (27)b | 1.30 (19)b |
| Antihypertensive drug            | 4.70 (68)a                   | 5.20 (75)b | 4.40 (66)a |
| Lipid-lowering drug              | 2.60 (38)a                   | 3.80 (55)b | 2.20 (33)a |
| **Physical measurements**        |                             |        |        |        |
| BMI (kg/m²)                      | 28.01 ± 4.58a                | 27.50 ± 4.57b | 27.95 ± 4.59a |
| WC (cm)                          | 95.68 ± 11.92a               | 94.36 ± 11.94b | 94.99 ± 12.31a |
| HC (cm)                          | 103.80 ± 9.02a               | 102.88 ± 8.94b | 103.47 ± 9.18a |
| WHR                              | 0.92 ± 0.07                  | 0.92 ± 0.07 | 0.92 ± 0.08 |
| WHTR                             | 59.55 ± 8.15a                | 58.77 ± 8.15b | 59.57 ± 8.39a |
| MAC (cm)                         | 30.51 ± 3.41a                | 30.20 ± 3.38b | 30.28 ± 3.4b |
| %BF                              | 33.77 ± 10.22a               | 33.02 ± 10.20a | 34.70 ± 10.14b |
| **Lipid and metabolic markers**  |                             |        |        |        |
| SBP (mm Hg)                      | 123.43 ± 18.60               | 122.48 ± 18.21 | 122.55 ± 18.76 |
| DBP (mm Hg)                      | 79.87 ± 11.25                | 79.57 ± 11.27 | 79.97 ± 11.47 |
| FBG (mg/dL)                      | 94.09 ± 40.53a               | 92.29 ± 38.94a | 89 ± 32.36b |
| Total cholesterol (mg/dL)        | 191.55 ± 37.61               | 192.27 ± 38.40 | 192.43 ± 39.41 |
| TG (mg/dL)                       | 124 (90, 177)                | 122 (86, 176.25) | 120 (83, 173) |
| LDL-C (mg/dL)                    | 117.99 ± 33.72               | 118.94 ± 34.81 | 119.80 ± 34.55 |
| HDL-C (mg/dL)                    | 41.34 ± 9.37b                | 42.10 ± 9.52ab | 42.43 ± 9.34b |
| Uric acid (mg/dL)                | 4.69 ± 1.37                  | 4.69 ± 1.40 | 4.67 ± 1.89 |
| Hs-CRP (mg/L)                    | 1.40 (0.90, 2.78)            | 1.39 (0.88, 2.63) | 1.47 (0.93, 2.78) |

Note: Dietary Inflammatory Index tertile ranges: T1: < −0.02; T2: ≥ −0.02 and < 1.18; T3: ≥ 1.18. Quantitative variables are expressed as mean ± standard deviation and categorical variables in absolute and relative values. Different letters indicate statistical significance on the same line. Values are determined using ANOVA or chi-square test.

Abbreviations: %BF, body fat percentage; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; HS-CRP, high-sensitivity C-reactive protein.; LDL-C, low-density lipoprotein cholesterol; MAC, mid-upper arm circumference; SBP, systolic blood pressure; TG, triglyceride; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.
### TABLE 2 Nutrient intake of participants according to the tertiles of Dietary Inflammatory Index

| Variables                  | T1 (n = 1434) | T2 (n = 1442) | T3 (n = 1489) |
|----------------------------|---------------|---------------|---------------|
| Energy (kcal/d)            | 2050.22 ± 566.44<sup>a</sup> | 2032.25 ± 579.37<sup>a</sup> | 1934.92 ± 562.36<sup>b</sup> |
| Carbohydrate (g/d)         | 153.03 ± 43.39 | 154.25 ± 44.39 | 153.26 ± 42.62 |
| Protein (g/d)              | 54.48 ± 11.70<sup>a</sup> | 53.81 ± 11.24<sup>b</sup> | 53.36 ± 11.22<sup>b</sup> |
| Total fat (g/d)            | 25.86 ± 15.17  | 25.89 ± 15.82  | 26.26 ± 15.64  |
| Saturated fat (g/d)        | 10.99 ± 8.28   | 11.09 ± 8.49   | 11.45 ± 8.69   |
| Polyunsaturated fat (g/d)  | 5.22 ± 1.67    | 5.13 ± 1.74    | 5.07 ± 1.83    |
| Monounsaturated fat (g/d)  | 27.33 ± 19.48<sup>a</sup> | 27.57 ± 22.37<sup>a</sup> | 25.58 ± 18.08<sup>b</sup> |
| Cholesterol (g/d)          | 131.07 ± 74.97 | 129.60 ± 74.69 | 129.57 ± 70.57 |
| Trans-fat (g/d)            | 0.04 ± 1.21    | 0.04 ± 1.28    | 0.04 ± 1.16    |
| Dietary fiber (g/d)        | 20.36 ± 7.69<sup>a</sup> | 19.49 ± 7.72<sup>b</sup> | 19.02 ± 7.63<sup>b</sup> |
| Iron (mg/d)                | 8.32 ± 2.55<sup>a</sup> | 7.98 ± 2.53<sup>b</sup> | 7.78 ± 2.49<sup>b</sup> |
| Magnesium (mg/d)           | 252.61 ± 67.21<sup>a</sup> | 245 ± 67.49<sup>b</sup> | 241.52 ± 65.14<sup>b</sup> |
| Copper (mg/d)              | 1.05 ± 0.35<sup>a</sup> | 1.03 ± 0.45<sup>a</sup> | 0.99 ± 0.30<sup>b</sup> |
| Zinc (mg/d)                | 6.37 ± 1.44<sup>a</sup> | 6.24 ± 1.44<sup>b</sup> | 6.16 ± 1.35<sup>b</sup> |
| Selenium (mg/d)            | 34.42 ± 12.90  | 34.59 ± 14.11  | 34.07 ± 19.43  |
| Vitamin D (mg/d)           | 0.59 ± 0.49    | 0.58 ± 0.49    | 0.59 ± 0.50    |
| Vitamin E (mg/d)           | 6.35 ± 8.53    | 6.09 ± 8.46    | 5.94 ± 7.22    |
| Vitamin B12 (mg/d)         | 2.91 ± 2.82    | 2.94 ± 3.79    | 2.74 ± 2       |
| Vitamin C (mg/d)           | 153.12 ± 116.51<sup>a</sup> | 139.45 ± 106.35<sup>b</sup> | 138.98 ± 106.41<sup>b</sup> |
| Retinol (mg/d)             | 163.52 ± 116.24, 230.34<sup>a</sup> | 166.78 ± 120.01, 238.46<sup>b</sup> | 169.73 ± 119.79, 240.52<sup>b</sup> |
| Carotene (mg/d)            | 2687.76 ± 1334.95<sup>a</sup> | 2497.12 ± 1240.97<sup>b</sup> | 2473.37 ± 1225.82<sup>b</sup> |

Note: Dietary Inflammatory Index tertile ranges: T1: < -0.02; T2: ≥ -0.02 and < 1.18; T3: ≥ 1.18. Quantitative variables are expressed as mean ± standard deviation and categorical variables in absolute and relative values. Different letters indicate statistical significance on the same line.

### TABLE 3 Prevalence ratio for Healthy Eating Index and dietary patterns according to the tertiles of the Dietary Inflammatory Index

| Outcome variables          | Model 1 PR (95% CI) | Model 2 PR (95% CI) | Model 3 PR (95% CI) |
|----------------------------|---------------------|---------------------|---------------------|
| HEI < 55                   | T1 1               | T2 1.11 (1.12-1.23)<sup>†</sup> | T3 1.14 (1.03-1.26)<sup>†</sup> |
| AHEI < 56.5                | T1 1               | T2 1.08 (0.98-1.19)<sup>†</sup> | T3 1.10 (0.99-1.21)<sup>†</sup> |
| DP Balanced                | T1 1               | T2 0.90 (0.81-1.00)<sup>**</sup> | T3 0.84 (0.75-0.93)<sup>**</sup> |
| DP Western                 | T1 1               | T2 0.98 (0.88-1.09)<sup>†</sup> | T3 0.93 (0.84-1.04)<sup>†</sup> |

Note: Abbreviations: AHEI, Alternative Healthy Eating Index; DP, dietary pattern; HEI, Healthy Eating Index; PR, prevalence ratio.

<sup>a</sup>Dietary Inflammatory Index tertile ranges: T1: < -0.02; T2: ≥ -0.02 and < 1.18; T3: ≥ 1.18. Model 1: adjusted for sex and age. Model 2: additionally adjusted for physical activity level, smoking status, marital cat, education cat, BMI, and WC. Model 3: additionally adjusted for diabetic drug, lipid-lowering drug and antihypertensive drug intake.

<sup>†</sup>P < .05.

<sup>**</sup>P < .01.
also considered a principal issue determination of outcomes. A large European cohort study showed a direct association between all-cause mortality, chronic heart disease, and DII in northern Europe. Scientists have proved that plant-based DP is beneficial for health and DII is not as strong as the MDS related to mortality rate in CVD. The relationship between CVD mortality and DII is weaker in older ages.

Few previous studies were focused on the relationship between DII, HEI, and AHEI, which are in agreement with our results. A cross-sectional study among 248 individuals aged greater than 20 years reported that DII was inversely associated with HEI. Inverse association between the most pro-inflammatory diet (higher DII) and healthier diets by calculating HEI and AHEI was also found. Furthermore, a cross-sectional study among college students found a negative correlation between DII and HEI.

Individuals in the third tertile of DII compared to the first tertile were more likely to have lower FBG, higher HDL-C, lower prevalence of diabetes, and lower anthropometric measurements including BMI, WC, HC, and MAC, while there was no significant association between DII and lipid profile including total cholesterol, triglyceride, low-density lipoprotein cholesterol, and BP. A higher DII was observed among older participants in the present study. Several studies have reported that a high FBG, or the presence of diabetes mellitus, was positively associated with DII. No significant correlation was obtained between DII with TG, HDL-C, and BP among a sample of Iranian adults. Denova-Gutiérrez et al reported that patients who were older and had a higher BMI had a more anti-inflammatory diet. No significant difference in BMI across DII score quartiles was found in our sample of Iranian adults. However, lower WC was found in the third quartile compared to the first quartile of DII score. Consuming a more healthy diet by these participants might be attributed to a change in diet according to the recommendation of a healthcare provider.

Individuals with a higher PAL had statistically higher DII values. One study demonstrated that those with greater weight and lower activity were most likely to have pro-inflammatory status. Controversially, in a research among young Columbian participants, PAL was not significantly associated with DII score. Since inconsistent associations have been reported in this regard, more studies are needed.

There are several strengths in the current study: first, the novelty of this study, as it is one of the first studies in Iran that has investigated the association between DII and healthy or unhealthy DPs by measuring HEI and AHEI; second, the large sample size; and third, adjustment for many potential confounding factors may provide a robust association between DII and diet. Although there are some limitations, DII has potential limitations which are related to the dietary regimens. Only 28 items of the FFQ among 45 food parameters were used for calculating DII were available; hence, it is possible that there are some missing data about unconsidered items. Finally, because of the type of study, which was cross-sectional, inferring the causality is difficult.

Further studies, preferably of cohort design, are necessary to access the relationship between DII and different methods assessing dietary habits including DP, HEI, and AHEI.

5 | CONCLUSION

There was a significant inverse association between DII, HEI, and AHEI. A negative association was found between the DII and adherence to balanced pattern as a healthy DP among a sample of Iranian middle-aged adults. According to mentioned strong points and restrictions in the present study, these results need more investigations to be confirmed. Our results also suggest that DII could be considered as an important dietary index, which is a useful tool to evaluate healthy eating of Iranian adults.

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AUTHOR CONTRIBUTIONS

We declare that we contributed significantly toward the research study, that is, Mostafa Saedi performed data analysis; Habibollah Esmiali, Hamid Reza Rahimi Seyed Mostafa Parizadeh, Mahdie Reza Jafarzadeh-Esfehani, Fateme Khorramruz, and Sajdeh Janandi conceived and interpreted the results; Maryam Mohammadi-Bajigian and Reza Zare-Feyzabadi designed the presented idea; Zahra Asadi, Roshanak Ghaffarian Zirak, and Mahdiye Yaghoooti Khorasani drafted the article; Maryam Tayefi developed the drafting of the article. Gordon A. Ferns, Nitin Shivappa, and James R. Hébert revised the article critically for important intellectual content; Hamideh Ghazizadeh and Majid Ghabour-Mobarhan approved the article; and Gordon A. Ferns and Majid Ghabour-Mobarhan supervised the project. Also, all authors read and approved the final article.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (Mums), Mashhad, Iran.

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