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**Diet variety mediates the relationship between appetite and micronutrient intake in patients with heart failure**

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Abstract

Aims: Eating a varied diet promotes adequate micronutrient intake. Poor appetite could decrease desire to eat a varied diet leading to dietary micronutrient insufficiencies. The interrelationships among appetite, diet variety, and dietary micronutrient intake have not been investigated in patients with heart failure. The purpose with the study was to determine whether the relationship between appetite and micronutrient insufficiency was mediated through diet variety.

Methods and results: A total of 238 patients with heart failure, mean age 61±12.1; 68% male and 45% NYHA class III/IV were included in this secondary analysis. Data collection consisted of a four-day food diary and self-reported appetite on a 10-point visual analog scale. Micronutrient insufficiency was defined as the total number of 17 minerals and vitamins that were insufficient in the diet. Diet variety was calculated as the number of 23 food types consumed over the 4 days. Mediation analysis, controlling for co-variates age, gender, NYHA-class and body mass index showed that diet variety mediated the relationship between appetite and micronutrient insufficiencies (indirect effect = -.0828, 95% CI: -.1585 to -.0150). There was no direct effect of appetite on micronutrient insufficiency (c´ = -.1802; 95% CI = -.3715 to .0111).

Conclusions: Diet variety played a previously unrecognized role in the relationship between appetite and dietary micronutrient intake in patients with heart failure. More research is needed to validate these associations in patients with heart failure.

Keywords: appetite, diet, heart failure, micronutrients

Novelty

- Decreased appetite is associated with low diet variety and micronutrient insufficiencies making it a risk factor for poor diet quality in patients with heart failure.

- Strategies to promote diet variety are important for increasing micronutrient intake in patients with heart failure, particularly those with decreased appetite.

## Introduction

Dietary micronutrient insufficiency is prevalent in patients with heart failure (HF). Estimates of dietary micronutrient insufficiencies in patients with HF range from 35-50%.[1-3] Insufficient nutritional intake is associated with poor mental and physical health[3,4], increased morbidity[5] and mortality.[6,7] Decreased appetite is a risk factor for malnutrition or undernutrition in older adults.[8] In patients with HF, who are primarily older adults, 49% of hospitalized patients with HF reported having decreased appetite and at least 22% experienced decreased appetite up to 18 months after discharge.[9] Decreased appetite typically leads to a diminished desire to eat a wide variety of foods. According to van der Meij,[10] about 22% of older adults experience poor appetite which has been associated with consuming relatively smaller serving sizes of food.[10] However, poor appetite may also be associated with micronutrient insufficiency in patients with HF.

Because no single food group provides all necessary nutrients, a limited variety of foods in the diet can lead to micronutrient insufficiencies.[11] A study of community-dwelling adults showed that up to 80% did not meet the estimated average requirement intake for calcium, magnesium, selenium, and zinc. Those consuming a more varied diet had a lower incidence of micronutrient deficiencies.[12] Results of a study with almost 6700 adults older than 64 years showed that those who reported high diet variety also reported high intakes of fiber, vitamins, and minerals suggesting that a varied diet contributes to higher dietary quality.[13] A varied diet has also been shown to be associated with increased food intake. In a small study of healthy young and older adults, the older adults consumed more when the diet had a great variety of foods.[14] On the other hand, older people exposed to a monotonous diet over a short period reported a lower desire to eat compared to younger people, which could contribute to poorer food intake and quality.[15] Researchers also reported that elderly people with a reduced appetite who eat a varied diet have higher energy intakes compared to people who do not

consume a varied diet.[16] Consequently, people with greater appetite would be expected to eat a more varied diet leading to a lower number of dietary micronutrient insufficiencies in patients with HF. Therefore, the purpose of this study was to explore whether appetite is linked with micronutrient insufficiency through their diet variety in patients with HF. We hypothesized that diet variety would play a mediator role in the association between appetite and micronutrient insufficiency.

## Methods

### Study design, sample, and settings

This was a secondary data analysis of a multicenter study approved by the Institutional Review Boards at each study site that conformed with the Ethical Principles for Medical Research Involving Human Subjects.[17] Participants received complete information about the study prior to providing written informed consent. Data from 265 patients with HF recruited from 3 outpatient HF academic clinics were used for secondary analysis.[6] Participants who were able to speak and write in English with confirmed stable HF and had New York Heart Association (NYHA) functional classification I-IV were eligible for the study. Participants with dietary restrictions other than those related to HF or diabetes were excluded. Of the initial sample of 274, thirty-six participants were excluded as they recorded intakes of less than 40% of the average required kcal intake during the 4 days of food diary data collection.[18]

### Measures

Appetite. In this study, appetite was defined as the overall urge or desire to eat that includes cravings for specific foods over the previous four days. Appetite was measured on a visual analog scale with the anchors of 1 “I had no appetite, no cravings” to 10 “my appetite was extremely good, strong cravings”. Data on appetite were collected the morning after completion of the 4-day diaries.

Micronutrient insufficiency. Food intake was measured by a 4-day food diary that was analyzed using Nutrition Data Systems-Research™ software. Participants received training on how to complete 4-day food diaries in their homes from a research nurse. They were provided a food diary, a digital food scale, food portion models, food portion pictures, and detailed instructions. Each participant performed a return demonstration to verify understanding. All foods and liquids consumed were recorded for 1 weekend day and 3 weekdays. All dietary supplements were also recorded and included in the analysis of micronutrient intake. The research nurse called the morning of the first recording day to verify understanding and answer any questions. Participants visited the clinical research center the morning following completion of food diary to review their diaries with a dietician.

Dietary adequacy of 17 micronutrients was determined according to recommendations of the Institute of Medicine Food and Nutrition Board.[19] The method for determining dietary micronutrient insufficiency is described in detail elsewhere.[6] In brief, a probability formula was used to determine whether, based on the 4-day food diaries, participants' diets were habitually deficient in magnesium, folate, vitamin B6, niacin, thiamin, riboflavin, and phosphorus. For calcium, iron, selenium, zinc, and vitamins $B_{12}$, C, D, and E, the averaged 4-day intake below the estimated average requirement (EAR) was defined as dietary insufficiency. For vitamin K and pantothenic acid, the averaged 4-day intake below 50% of the recommended daily allowance (RDA) was defined as dietary micronutrient insufficiency. The total number of these 17 micronutrients defined as insufficient was used for analyses.

Diet variety. The number of servings of 23 food subgroups consumed over 4 days were derived from the food diary analysis: fruits, green vegetables, yellow vegetables, other vegetables, tomatoes, potatoes, legumes, loaf bread, pasta, cereal, beef/veal, lamb, pork, poultry, fish, shellfish, cold cuts, organ meats, eggs, nuts, milk, cheese, and yogurt. Diet

variety was defined as the total number of food subgroups of which at least one serving was consumed over the 4 days, with a possible range of 1 to 23.

Sample characteristics. We collected sociodemographic characteristics using a structured questionnaire, including age, sex, ethnicity, and civil status. We also collected clinical information (i.e., NYHA class, left ventricular ejection fraction, prescribed medications, and body mass index) through patient interviews and review of patients' medical records.

Statistical analysis

We selected only participants with no missing values of the variables (i.e., micronutrient insufficiency, diet variety, and appetite) included in this secondary analysis. Descriptive statistics, including frequency, percentile, mean, and standard deviation, were conducted to describe samples' demographic and clinical characteristics and variables' characteristics. We also conducted comparison in age, gender, and NYHA class between the participants who were selected and who were excluded in this secondary study using independent t-test and Chi-square to examine sample selection bias. Bivariate associations among variables selected for mediation analysis were examined by conducting Pearson correlation, Spearman correlation, and Chi-square depending on the measurements. We conducted two mediation analyses by Heyes' PROCESS macro program (version 3.5)[20] with 5,000 bootstrap samples. First mediation analysis was conducted without covariates. The second mediation analysis was conducted controlling for age, gender, New York Heart Association (NYHA), and body mass index. These covariates have been reported to have an effect on nutrition intake and appetite. [12,21,22] The PROCESS macro program (Model 4) generated direct, indirect, and total effects of appetite on micronutrient insufficiency. The indirect effect indicated a mediation effect of diet variety (i.e., mediator) on the association between appetite and micronutrient insufficiency. Direct effect (*c´)* indicated an effect of appetite on nutrition insufficiency, and total effect indicated the sum of direct and indirect effects (a*b) of appetite. A 95% bootstrap

confidence interval determined the statistical significance of such effects. Multiple regressions results generated by the PROCESS macro were also reported to explain the mediation model. All statistical analyses were conducted using the SPSS version 27 with an alpha of 0.05.

## Results

### Sample characteristics

Of the 265 participants in the parent study, 27 were excluded resulting in a final sample of 238 participants (mean age 61 ± 12; male n=164, 68%; NYHA III/IV, n=107, 45%). There was no mean age difference between the selected and the excluded participants (61.35 vs. 61.07, respectively, P = .910). The proportion of gender (Fisher's exact test P =.086) and NYHA class (Fisher's exact test P= .054) were similar between the two groups. Participants were not underweight based on BMI 30 kg/$m^2$ (SD=7). The median appetite score was 8 (IQR=4). The mean number of micronutrient insufficiencies was 4.7 (SD= 3.5) and the mean diet variety score was 12.4 (SD=2.6.) Table 1. Table 2 presents correlations among variables. Micronutrient insufficiency was negatively correlated with diet variety, appetite, and age (r = -.207 to -.344, P < .001) and positively correlated with NYHA class (r = .182, P < .001). Diet variety was positively correlated with appetite (r = .230, P <.001) and age (r = .143, P < .05). Gender and NYHA class were not associated (Fisher's exact test P= .484).

### Effect of appetite on micronutrient insufficiency

In the multiple regression without covariates (Tabel 3), appetite and diet variety were strong predictors of micronutrient insufficiency by explaining 13.5% of the variance (P <.001). In mediation analysis, appetite had a direct, negative effect on micronutrient insufficiency ($c´$ = -.2018, 95% CI= -.3898 to -.0138). There was a significant indirect effect of appetite on micronutrient insufficiency through diet variety (a*b = -.1089, 95% bootstrap CI= -.1862 to -.0385).

Table 4 presents the second mediation model with covariates (i.e., age, gender, NYHA class, and body mass index). The model explained 16% of the variance in micronutrient insufficiency (P < .001). The indirect (mediator) effect of appetite through diet variety on the micronutrient insufficiency remained significant (a*b effect = -.0828, 95% CI: -.1585 to -.0150). Patients who had higher appetite ratings had a more varied diet ($a_1$ = .2315, P <.001), with higher diet variety associated with a lower micronutrient insufficiency ($b_1$ = -.3578, P <.001). There was no definitive evidence that appetite was directly associated with micronutrient insufficiency ($c´$ = -.1802; 95% CI = -.3715 to .0111). Figure 1 present each path and summary of mediation analysis.

**Discussion**

The findings of this study demonstrated that diet variety mediated the association between appetite and dietary micronutrient insufficiency. As predicted, higher appetite was associated with greater dietary variety, which was associated with a lower number of dietary micronutrient insufficiencies. Given that inadequate micronutrient intake and poor appetite have negative consequences on patients' health outcomes,[6,23] appetite and dietary variety may need to be considered important to assess to improve quality of dietary intake.

Two studies including 6647 overweight non-cardiac Mediterranean adults and 4537 children showed that a varied diet was associated with increased diet quality related to intake of proteins, vitamins, minerals.[13,24] Other researchers have also shown that a varied diet can improve the intake of both micro- and macronutrients based on data obtained from a National Health and Nutrition Examination Survey of nearly 4000.[25] These results are consistent with our findings, suggesting that the relationship of diet variety to nutritional intake is universally important and not limited to people with HF.

While we showed that appetite influences nutritional intake through diet variety, others have shown that increasing diet variety can improve nutritional intake. Wijnhoven et al[16]

demonstrated in a small study of older women with reduced appetite that energy intake could be increased by providing a diet with a greater variety of foods. This suggests that there may be a complex relationship with increased appetite improving diet variety and increased diet variety improving food intake.[6,23] The Mediterranean style diet and Dietary Approaches to Stop Hypertension (DASH) diet have been recommended for people with HF, including those with comorbid diabetes.[26] These diets are low in sodium, nutritionally complete, and high in antioxidants. From the perspective of this study, they have the additional advantage of providing a highly varied diet, which can be helpful in addressing poor appetite in patients with HF. Thus, health care professionals can use these diets as examples of the varied types of foods patients with HF can eat to increase diet variety.

In the unadjusted mediation analysis there was a direct, negative association between appetite and dietary micronutrient insufficiencies. Similar findings were reported in cross-sectional studies using different methods to assess appetite and food intake [10,27] suggesting this is a robust finding. In the adjusted mediation analysis, the effect of appetite on micronutrient insufficiency was indirect being mediated through diet variety. This finding suggests that the relationship between appetite and micronutrient insufficiency involves diet variety. Consequently, poor appetite appears to be an important contributing factor for nutrition inadequacy.[28-30] Understanding the underlying factors affecting appetite in this population is an important next step in developing interventions to improve nutritional intake.

The role of diet variety in nutritional intake of people with HF has not been previous explored. In other populations, food intake and diet variety have been measured several ways.[11] The common method was by food frequency questionnaires, which provide data on recall estimates of foods consumed over extended periods of time. The next most common method was single or two-day 24-hour recalls, which provide limited data on daily differences in variety of foods consumed. Diet variety has been defined as number of different foods

consumed over extended periods of time, or number of foods consumed within specific meals, or number of foods consumed within a limited number of food groups (e.g., healthy vs, unhealthy). We identified one other study in which food intake was measured using 4-day food diaries in a group of people enrolled in a weight management program.[31] However, diet variety was defined as different foods consumed within each macronutrient category (carbohydrate, fat, and protein). Our method measured actual foods consumed over a 4-day period, which provided data on day-to-day variation of foods consumed. Our definition of diet variety was based on consumption of 23 different food groups, among the most comprehensive assessments of diet variety to date.

## Limitations of the study

Men comprised the majority of the sample. Caution should be used when generalizing to women. Participants were also slightly younger than the normal population with HF. To address these limitations, analyses were adjusted for age and gender. The sample was also primarily White, which may limit generalization to other populations of people with HF. Participants rated their appetite on a visual analog scale, which measured their overall perception of their appetite. It didn't capture other related factors that influence appetite, such as early satiety, decreased taste, and anhedonia. We adjusted for age, gender, NYHA class and BMI in this secondary data analysis due to limited data availability. Other factors that likely affect appetite or eating habits (e.g., habitual dietary pattern, food accessibility, and food insecurity) should be included in future research to increase our understanding of the role of appetite in nutritional quality diets of patient with heart failure.

## Conclusion

The results of this study provide evidence that both appetite and diet variety influence micronutrient intake. Current HF guidelines do not include recommendations for how to

improve nutrition in HF due to lack of evidence.[32] Assessment of appetite and diet variety should be added to future research aimed at improving nutritional intake in patients with HF.

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Conflict of interest: The authors declare no conflict of interest.

Data availability

The data underlying this study will be shared on reasonable request to the corresponding author with permission of the second author, T. A. Lennie.

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Table 1. Sample characteristics (N=238)

| | |
|---|---|
| Age year, mean (SD) | 61.3 (12.1) |
| Sex, n (%) | |
| Male | 164 (68.9) |
| Female | 74 (31.1) |
| Ethnicity, n (%) | |
| White | 175 (73.5) |
| Other ethnicity | 63 (26.5) |
| Civil status, n (%) | |
| Married/Co-habitation | 143 (60.1) |
| Single/divorced/widowed | 95 (39.9) |
| NYHA classification III/IV, n (%) | 107 (45.0) |
| LVEF, mean (SD) <40% | 34.6 (0.49) |
| Medication, n (%) | |
| ACEI | 161 (67.6) |
| ARB | 46 (19.3) |
| β-blocker | 209 (87.8) |
| Aldosterone antagonist | 57 (23.9) |
| Diuretics | 177 (74.4) |
| Body Mass Index, kg/m2, mean (SD) | 30.3 (7.0) |
| Appetite, VAS-scale, median (IQR) | 8.0 (4.0) |
| Micronutrient insufficiency, mean (SD) | 4.7 (3.5) |
| Diet variety, mean (SD) | 12.4 (2.6) |

SD, standard deviation; NYHA classification, New York Heart Association (NYHA) functional classification; LVEF, left ventricular ejection fraction; ACEI, angiotensin-converting enzyme inhibitor; ARB, Angiotensin-II-receptor blocker; VAS-scale, Visual Analog Scale.

Table 2. Correlation among variables

| | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1. Dietary insufficiency | | | | | | |
| 2. Diet variety | -.344** | | | | | |
| 3. Appetite | -.206** | .230** | | | | |
| 4. Age | -.207** | .143* | .080 | | | |
| 5. Gender | -.125 | -.015 | -.105 | -.018 | | |
| 6. NYHA class | .182** | -.140* | -.269** | -.044 | | |
| 7. Body mass index | .110 | -.097 | -.111 | -.196** | .083 | .185** |

Note: Gender; male = 0, female = 1; NYHA class: I-II = 1, III-IV = 2

Table 3. Effect of appetite on micronutrient insufficiency without covariates

A. Multiple regression predicting nutritional insufficiency

| | B | SE | Beta | p-value | 95% lower CI | 95% upper CI | Model fit |
|---|---|---|---|---|---|---|---|
| Appetite | -.2018 | .0954 | -.1321 | .0355 | -.3898 | -.0138 | $R^2$ = .1347; |
| Diet variety | -.4100 | .0816 | -.3138 | <.0001 | -.5708 | -.2493 | F=18.22;P <.0001 |

B. Effects of the appetite

| | Effects | SE | t-value | P-value | 95% lower CI | 95% upper CI |
|---|---|---|---|---|---|---|
| Direct effect | -.2018 | .0954 | -2.15 | .0355 | -.3898 | -.0138 |
| Indirect effect | -.1089 | .0380 | - | - | -.1862 | -.0385 |
| Total effect | -.3107 | .0976 | -3.1839 | .0016 | -.50300 | -.1185 |

Table 4. Effect of appetite on micronutrient insufficiency with covariates

A. Final multiple regression predicting micronutrient insufficiency

| | B | SE | Beta | p-value | 95% lower CI | 95% upper CI | Model fit |
|---|---|---|---|---|---|---|---|
| Appetite | -.1802 | .0971 | -.1176 | .0648 | -.3715 | .0111 | $R^2$ = .1662; |
| Diet variety | -.3578 | .0814 | -.2738 | <.00001 | -.5181 | -.1975 | F=8.7337; |
| Age | -.0443 | .0178 | -.1531 | .0132 | -.0793 | -.0094 | P <.0001 |
| Gender (ref = male) | -.9664 | .4491 | -.1297 | .0325 | -1.8514 | -.0815 | |
| NYHA (ref= I & II) | .6999 | .4360 | .1007 | .1098 | -.1591 | 1.5590 | |
| Body mass index | .0307 | .0307 | .0337 | .5875 | -.0438 | .0772 | |

B. Effects of the appetite

| | Effects | SE | t-value | P-value | 95% lower CI | 95% upper CI |
|---|---|---|---|---|---|---|
| Direct effect | -.1802 | .0971 | -1.8558 | .0648 | -.3715 | .0111 |
| Indirect effect | -.0828 | .0368 | - | - | -.1585 | -.0150 |
| Total effect | -.2630 | .0990 | -2.6575 | .0084 | -.4580 | -.0680 |

Figure 1. Effect of appetite on micronutrient insufficiency