Original Article

Dimethylarginines in acute myocardial infarction: Association with lifestyle, sociodemographic, and somatometric factors

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Abstract

Background: Recent findings associate asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) with the prognosis of acute myocardial infarction (AMI). The purpose of the current study was to associate patients' lifestyle, sociodemographic, and somatometric characteristics with the time course of ADMA and SDMA concentrations in the serum of AMI patients. **Patients and Methods:** In the serum of 66 AMI patients, ADMA, SDMA, troponin T, and C-reactive protein (CRP) were measured upon hospital admission (<24 h) and on the 3rd day following. Lifestyle, sociodemographic, and somatometric characteristics were obtained through a questionnaire, filled on patient discharge. **Results:** ADMA concentrations on the 1st day positively correlated with daily reported hours of sleep (+0.497, $P < 0.001$) and delivery or eating out frequency (+0.285, $P = 0.02$), whereas it negatively correlated with reported physical condition (-0.304, $P = 0.013$). A personal history of hypertension indicated higher 1st-day ADMA concentration (1.818 vs 1.568, $P = 0.042$). Age positively correlated with 1st-day SDMA (+0.320, $P = 0.009$). All of the biomarker concentrations were reduced on the 3rd day measurements ($P < 0.001$). Self-reported lifetime minimum BMI positively correlated with either absolute (r = +0.366, $P = 0.009$) or percentage (r = +0.262, $P = 0.045$) ADMA reduction. A daily sleep in 5–8-h range was inversely correlated with percentage (-0.410, $P = 0.001$) or absolute (r = -0.369, $P = 0.002$) SDMA reduction. **Conclusions:** Modifiable factors such as BMI, eating habits, physical condition, and sleep seem to affect the baseline levels or time course of ADMA and SDMA in AMI patients. Changes in these factors may affect AMI prognosis by altering dimethylarginine levels.

Keywords: Asymmetric dimethylarginine (ADMA), diet, myocardial infarction, obesity, prognosis, symmetric dimethylarginine (SDMA)

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Introduction

Acute myocardial infarction (AMI) constitutes a highly frequent and life-threatening cardiac emergency, requiring immediate medical attention.[1] Myocardial infarction is defined as "the

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presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia".[2] Troponins are essential biomarkers in the diagnosis of AMI.[3] C-reactive protein (CRP) is another well-studied marker involved in every stage of cardiovascular disease, from atherogenesis to clinical outcomes.[4]

Asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) are amino acids intracellularly produced by the posttranslational modification of the L-arginine.[5] In AMI patients, ADMA baseline levels on the 1st day (<24 h) of hospital admission were found to be predictive of mortality on a 1-year follow-up.[6] Concerning SDMA, it is implicated with an altered ventricular ejection fraction of AMI patients, which leads to worse hospital outcomes and it has also been proposed as a therapeutic target in ischemic heart disease.[7,8]

Due to the possible critical involvement of ADMA and SDMA in AMI's progression and morbidity, we sought to monitor these markers on the 1st day (<24 h) of admission and on the 3rd post-admission day. Besides, we aimed to identify somatometric, demographic, and lifestyle factors that have an impact on the serum concentration levels of these dimethylarginines upon admission, as well as to assess their reduction or increase on the 3rd day with the presence of these factors.

Material and Methods

Study population

The current study included 66 consecutive patients admitted for AMI in the Cardiology Department of General Hospital of Chalkida in Greece. Patient inclusion criteria were:

- Confirmed occurrence of AMI
- Age between 30 and 75 years
- Absence of chronic inflammatory and autoimmune disease, diabetes, renal failure, cancer, or any other disease that could severely affect stress markers

Questionnaire development and distribution

The participants completed a questionnaire with questions including:

- Sociodemographic characteristics: age, sex, education, occupation, employment status, place of birth
- Somatometric characteristics: weight (current and self-reported lifetime maximum and minimum), height
- Family history: dyslipidemia, hypertension, cardiovascular event
- Patient history: the presence of dyslipidemia, hypertension
- Feelings of high anxiety (yes/no) and anxiety evaluation on an ascending scale of 1 to 7.
- Sleep: hours of sleep per day, daily napping
- Smoking (currently, ex, passive, never) and alcohol consumption (frequency and type of beverage)
- Self-reported physical condition on a scale of 0 (bad) to 4 (excellent), physical requirements for work on a scale of 0 (none) to 4 (excessive)
- Diet: Following a special type (e.g., low cholesterol), eating out/delivery food consumption frequency (never to daily), daily sugar consumption in beverages/coffee (in teaspoons), dairy consumption, frequency of eating between meals, preference in biologic products, daily water consumption (in glasses)

The questionnaire was in paper form and its completion required approximately 15 min. The patient filled it on the day of discharge.

Blood measurements

Blood samples from 66 patients were obtained < 24 h after admission (1st day). On the 3rd day post-admission, a second blood sample was obtained. Blood was centrifuged and serum was stored at -80°C for future analysis. On each blood sample, troponin T, CRP, ADMA, and SDMA concentrations were measured in the serum. CRP and troponin were promptly available from the laboratory results of the hospital. Quantitative determination of ADMA and SDMA was obtained through competitive enzyme-linked immunosorbent assay (ELISA).

Statistical analysis

Statistical analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) 23 statistics software program. Nominal data are described through frequencies/percentages whereas continuous variables, median, or mean and minimum/maximum values are presented. For continuous variables, independent samples *t*-test or the nonparametric Mann-Whitney U test was utilized, depending on the occasion. A comparison between 1st and 3rd-day biomarker measurements was conducted through the Wilcoxon signed-rank test. Concerning correlations in continuous variables, Spearman's (nonparametric) correlation coefficient was calculated. The statistical significance threshold of the current study was set at $P < 0.05$.

Results

Regarding patient population characteristics, the median age was 64 (range: 41–70) with 27% (18/66) being females. A positive history for hypertension was present in 67% of patients (44/66) and positive history for dyslipidemia was present in 41% (27/66) of patients. About 58% were current smokers, whereas 3% ex. Height and current weight were available in 59/66 patients, which allowed us to calculate body mass index (BMI). Patients' mean BMI at the time of the study was 26.63 ± 1.67 kg/m^2 (21.7–30.9), whereas mean lifetime minimum BMI was 24.84 ± 1.77 kg/m^2 (range: 20.1–29.4) and mean lifetime maximum was 27.9 ± 1.6 kg/m^2 (range: 23–32.2).

Association and correlation of 1st-day marker concentration levels with several factors

Statistically significant correlations of the examined biomarkers occurred with reported total daily sleeping hours, weekly eating

out/delivery food consumption frequency, self-reported physical condition status, age, and daily sugar in coffee consumption. Table 1 presents the correlation coefficients as well as the statistical significance of these results.

Furthermore, regarding hypertension, 12 patients reported an unknown history. Of the remaining 54, a positive medical history of hypertension indicated higher ADMA upon admission when compared to a negative one (1,818 ± 0,432 vs 1,568 ± 0,437, $P = 0.042$).

1st and 3rd-day marker concentration comparison

Between the 1st and 3rd day, a statistically significant decrease in all four markers was observed ($P < 0,001$), as presented in Table 2. Nonetheless, we observed that ADMA increased in 10/66 patients whereas, in SDMA, the respective fraction was 14/66. After dividing the patients into two groups, those with an increase in ADMA levels had decreased weight (either current or lifetime self-reported maximum-minimum) and height. Regarding SDMA, patients with increased SDMA levels slept more on average in comparison to patients with reduced levels. Table 3 presents the resulting differences among the two groups as well as their statistical significance.

Factors affecting ADMA and SDMA reduction

Among patients, different ADMA and SDMA reductions occurred. We expressed these reductions either as total (e.g., ADMA 1st day – ADMA 3rd day) or as a reduction percentage (e.g., [ADMA 1st day – ADMA 3rd day/ADMA 1st day] × 100%). We subsequently examined several factors of the questionnaire concerning the occurring reductions. Spearman's' rho correlation indicated that self-reported lifetime low BMI was positively correlated with ADMA reduction ($r = +0.366$, $P = 0.009$) or ADMA reduction percentage ($r = +0.262$, $P = 0.045$). As a result, a higher reduction in ADMA occurred in individuals with higher minimum lifetime BMI, as shown in Figure 1.

In SDMA reduction, statistically significant correlations occurred when examining the daily sleep hours of patients. However, 65/66 patients reported sleeping between 5–8 h per day, whereas only one reported sleeping 9 h. Therefore, the latter was not introduced into the calculation. Spearman's' rho correlation revealed a negative correlation between SDMA decrease and 5–8 daily hour sleep, either as absolute decrease ($r = -0.369$, $P = 0.002$) or as a percentage ($r = -0.410$, $P = 0.001$). Patients sleeping fewer hours had greater SDMA decrease in comparison to patients sleeping more hours, as presented in Figure 2.

Discussion

This is the first study comparing ADMA/SDMA concentrations with several demographic and lifestyle characteristics of AMI patients on the 1st admission and the 3rd post-admission day. After measuring ADMA and SDMA circulating concentrations on 1st and 3rd-day post-admission for AMI, a statistically significant decrease in both toxic amino acids was revealed. Considering that the same was observed regarding troponin and CRP concentration levels, one could hypothesize that their decrease was expected as part of patients' clinical remission.

Over the past decades, prospective clinical studies among different patient populations have established a solid relationship between ADMA and cardiovascular risk. The predominant mechanism of action is via inhibiting NO synthesis and impairing the beneficial, vasodilatory impact of NO in normal vascular tone.[9] Following reported literature outcomes, we noticed that patients with a positive medical history of hypertension had higher ADMA levels upon admission.[10] Analogous observations were detected among patients with bad eating habits, possibly due to simultaneous, underlying comorbidities associated with disrupted lipid levels and oxidative stress. Additionally, a negative correlation occurred with self-reported physical condition status, highlighting the possible protective effect of an active lifestyle. SDMA did not correlate with any of the lifestyle factors addressed in the questionnaire. Nonetheless, a positive correlation between 1st-day SDMA and age was observed. SDMA

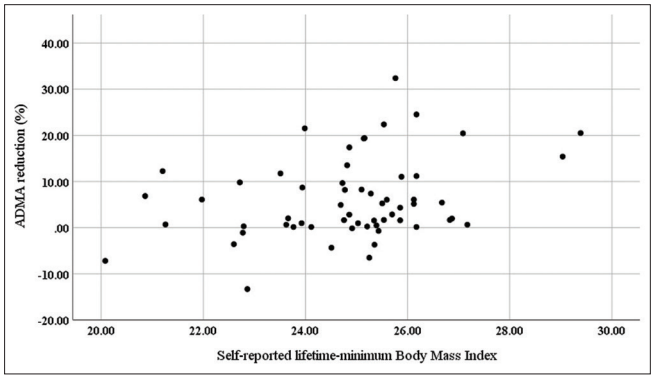

Figure 1: Scatterplot depicting self-reported lifetime-minimum body mass index (kg/m²) in X-axis about ADMA reduction expressed as a percentage of the baseline (% of 1st day) concentration on the Y-axis

Table 1. Factors correlating with 1st day (admission) biomarker concentrations

	Sleeping hours	Delivery Food/Eating out the frequency	Physical Condition	Age	Sugar in coffee
ADMA	+0.497, (P<0.001*)	+0.285, (P=0.02*)	-0.304, (P=0.013*)	-	-
SDMA	-	-	-	+0.320, (P=0.009*)	-
Troponin	-	-	-	+0.274, (P=0.027*)	-
CRP	-	-	-	-	+0.257, (P=0.037*)

*Spearman's rho correlation coefficient

Table 2: Comparison between 1st and 3rd-day biomarker concentrations

	1st Day (admission)	3rd Day	*P*
ADMA (μmol/L)	1.719±0,451	1.615±0.463	<0.001*
SDMA (μmol/L)	0.735±0,268	0.659±0.232	<0.001*
Troponin (μg/L)	1.203±1,421	0.878±1.153	<0.001*
CRP (mg/L)	47.359±10,571	37.902±9.219	<0.001*

*Wilcoxon signed-rank test

Table 3: Resulting different characteristics of patients with ADMA or SDMA increase

	Reduction	Increase	*P*
ADMA (number of patients)	56/66	10/66	
Max-reported weight (kg)	84.16±7.885	79.56±6.444	0.030*
Min-reported weight (kg)	77.27±7.634	69.11±8.146	0.015*
Weight (kg)	82.45±7.654	76.44±6.307	0.025**
Height (m)	1.757±0.058	1.703±0.052	0.022**
SDMA (number of patients)	52/66	14/66	
Daily sleep (h)	6.67±0.879	7.29±0.726	0.016*

*Independent samples Mann-Whitney U test **Independent samples *t*-test

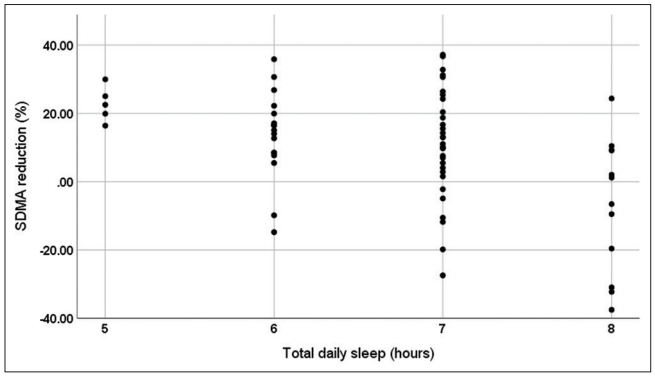

Figure 2: Scatterplot depicting total daily hours of sleep on the X-axis and SDMA reduction expressed as a percentage of the baseline (% of 1st day) concentration on the Y-axis

is an endogenous marker of renal function and correlates highly with GFR, explaining the accumulation in older patients who are at an increased risk of renal dysfunction.[11] A similar positive correlation was observed regarding 1st-day troponin levels and age, possibly explaining why the conventional cut-off value of troponin for AMI diagnosis provides low specificity in the elderly.[12] Notably, SDMA reduction was inversely correlated with total daily sleep duration. In the 5–8 sleep hours range which we were able to study, patients sleeping more had lower SDMA reduction. Besides, patients with an increase in SDMA between 1st and 3rd day slept more on average (7,29 vs 6,67 hours per day). To interpret these findings, we need to consider three facts:

- The predominant excretion of SDMA occurs via the kidneys and may even be a marker of glomerular filtration rate (GFR).[11,13]
- Previous research findings report that kidney function is associated with a U-shape when considering self-reported daily sleep hours. At extreme sleep hours, (<6 or > 9) kidneys tend to hyperfiltrate.[14-17] Notably, this U- shape is more evident in older individuals (>65 years old) and one study concluded that for each 1 h decrease in sleep duration an increase of 1.5 mL/min/1.73 m^2 in GFR occurs over a decade (estimated from creatinine clearance).[15,16]
- We only had one patient reporting a daily sleep of 9 h, therefore, we could only report results in the 5–8-h range.

As a result, considering that SDMA is mainly excreted via the kidneys and that GFR increases with less sleep, our results are in accordance with the literature. Nonetheless, we could not exhibit or examine the previously mentioned U-shaped correlation, due to the lack of patients sleeping 9 h or more. Besides, our results revealed a positive correlation of 1st-day ADMA concentrations with reported total daily sleeping hours. Findings connecting ADMA and its degrading enzyme, dimethylarginine dimethylaminohydrolase (DDAH), with sleep parameters or disorders do exist.[18-20] Nonetheless, we were not able to identify a possible underlying mechanism to explain this correlation. We should also note that the data analyzed about sleep were self-reported and thus we could not assess sleep quality. The interrelationship of sleep and biomarkers is complex and difficult to investigate; further studies with more meticulous sleeping hours and quality estimation are needed to confirm these findings and investigate the underlying mechanisms.

Concerning AMI mortality, as mentioned, ADMA concentration levels on the 1st day of admission are considered as a prognostic factor.[6] Furthermore, among individuals with higher BMI, an obesity paradox exists; a higher BMI correlates with better clinical outcomes.[21] This could explain our observation that individuals who maintain a higher lifetime-minimum BMI have a greater decrease in ADMA. Since ADMA is a toxic amino acid, a faster elimination could indicate a prompter clinical remission of AMI. Besides, the only relevant study examining ADMA, BMI, and mortality, recruited a total of 4164 patients with suspected angina pectoris and reported that ADMA is associated with AMI mortality only in individuals with lower BMI (≤ 26.3 kg/m^2). This indicates a disassociation of ADMA and mortality on higher BMI patients.[22] Besides, measured ADMA levels were unexpectedly increased on the 3rd post-admission day in only 10/66 patients. These patients weighed less and had a shorter height, with no observations occurring concerning BMI. However, these results again point out to an implication of somatometric characteristics in the course of ADMA concentration levels during AMI. Finally, our study revealed a statistically significant correlation between 1st-day CRP and daily sugar consumption in coffee. This can be considered as an anticipated outcome, considering that sugar consumption in beverages has been shown to promote inflammation.[23]

Summary of key findings

Hypertension, bad eating habits, more daily hours of sleep, and worse physique were associated with higher ADMA baseline levels in the onset of AMI, whereas regarding SDMA, only increased age correlated with increased baseline levels.

Comparing the biomarkers' concentration levels between the 1st and 3rd day of hospital admission for AMI, both were observed to significantly reduce, on average. Finally, patients maintaining a higher lifetime-minimum BMI exhibited greater reduction in ADMA concentration levels, whereas patients sleeping less (in the 5–8-h range) showed greater SDMA reduction.

Limitations

The relatively small patient database was a limitation for our study, as well as that the questionnaire data collected were self-reported. However, a major strength of this study is that we managed to investigate and study a wide variety of sociodemographic, lifestyle, and somatometric factors.

Implications for primary care practice

AMI prognosis has been reported to be affected by ADMA and SDMA concentration levels[6,7]; thus, the knowledge that lifestyle and somatometric factors affect these biomarkers may help and guide accordingly primary and hospital care physicians in taking early appropriate action and informing their patients on modifiable factors associated and related with worse outcomes in case of AMI occurrence. Initially, clinicians could increasingly advocate and promote good eating habits, physical exercise, and proper control of hypertension on all patients, since these factors seem to correlate with lower baseline levels of ADMA during AMI. Furthermore, maintaining a normal weight should always be recommended, since obese patients are generally an at-risk group for AMI occurrence.[24]

Conclusion

Overall, all of the investigated marker concentrations seem to decrease on the 3rd post-admission day, probably as a result of patients' clinical remission. In general, ADMA and SDMA are reported to affect AMI's prognosis. Interestingly, interventional factors such as sleep duration, BMI, eating habits, physical condition seem to alter their concentration levels during AMI and, therefore, possibly influence prognosis via altering dimethylarginine levels. Larger confirmatory studies and future research could provide more details on these very significant findings and results.

Ethics approval

The study protocol was approved by the Scientific Committee of the General Hospital of Chalkida, Evia, Greece. Informed consent was obtained from all individual participants included in the study.

Consent to publish

All individual participants consented to the publication of the data obtained.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Anderson JL, Morrow DA. Acute myocardial infarction. N Engl J Med 2017;376:2053-64.
2. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al.* Fourth universal definition of myocardial infarction (2018). Circulation 2018;138:e618-51.
3. Aydin S, Ugur K, Aydin S, Sahin İ, Yardim M. Biomarkers in acute myocardial infarction: Current perspectives. Vasc. Health Risk Manag 2019;15:1-10.
4. Calabro P, Golia E, T.H. Yeh E. Role of C-reactive protein in acute myocardial infarction and stroke: Possible therapeutic approaches. Curr Pharm Biotechnol 2011;13:4-16.
5. Tain YL, Hsu CN. Toxic dimethylarginines: Asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA). Toxins (Basel) 2017;9:92.
6. Zeller M, Korandji C, Guilland J-C, Sicard P, Vergely C, Lorgis L, *et al.* Impact of asymmetric dimethylarginine on mortality after acute myocardial infarction. Arterioscler Thromb Vasc Biol 2008;28:954-60.
7. Lorin J, Guilland JC, Stamboul K, Guenancia C, Cottin Y, Rochette L, *et al.* Increased symmetric dimethylarginine level is associated with worse hospital outcomes through altered left ventricular ejection fraction in patients with acute myocardial infarction. PLoS One 2017;12:e0169979.
8. Djordjević BV, Pavlović R, Ćosić V, Deljanin-Ilić M, Ristić T, Krstić N, *et al.* High clinical accuracy of asymmetric dimethylarginine and symmetric dimethylarginine in patients with ischemic heart disease. Amino Acids 2012;43:2293-300.
9. Böger RH. Asymmetric dimethylarginine (ADMA): A novel risk marker in cardiovascular medicine and beyond. Ann Med 2006;38:126-36.
10. Perticone F, Sciacqua A, Maio R, Perticone M, Maas R, Boger RH, *et al.* Asymmetric dimethylarginine, L-arginine, and endothelial dysfunction in essential hypertension. J Am Coll Cardiol 2005;46:518-23.
11. Kielstein JT, Salpeter SR, Bode-Boeger SM, Cooke JP, Fliser D. Symmetric dimethylarginine (SDMA) as endogenous marker of renal function—a meta-analysis. Nephrol Dial Transplant 2006;21:2446-51.
12. Ichise T, Tada H, Sakata K, Kawashiri MA, Yamagishi M, Hayashi K. Impact of aging on high-sensitivity cardiac troponin T in patients suspected of acute myocardial infarction. Intern Med 2017;56:2097-102.
13. Kielstein JT, Veldink H, Martens-Lobenhoffer J, Haller H, Burg M, Lorenzen JM, *et al.* SDMA is an early marker of change in GFR after living-related kidney donation. Nephrol Dial Transplant 2011;26:324-8.
14. Yamamoto R, Nagasawa Y, Iwatani H, Shinzawa M, Obi Y, Teranishi J, *et al.* Self-reported sleep duration and prediction of proteinuria: A retrospective cohort study. Am J Kidney Dis 2012;59:343-55.
15. Petrov ME, Kim Y, Lauderdale DS, Lewis CE, Reis JP, Carnethon MR, *et al.* Objective sleep, a novel risk factor for alterations in kidney function: The CARDIA study. Sleep Med 2014;15:1140-6.
16. Yu JH, Han K, Kim NH, Yoo HJ, Seo JA, Kim SG, *et al.*

U-shaped association between sleep duration and urinary albumin excretion in Korean adults: 2011-2014 Korea National Health and Nutrition Examination Survey. PLoS One 2018;13:e0192980.

17. Ye Y, Zhang L, Yan W, Wang A, Wang W, Gao Z, *et al.* Self-reported sleep duration and daytime napping are associated with renal hyperfiltration and microalbuminuria in an apparently healthy Chinese population. PLoS One 2019;14:e0214776.
18. Amrouni D, Meiller A, Gautier-Sauvigné S, Piraud M, Bouteille B, Vincendeau P, *et al.* Cerebral changes occurring in arginase and dimethylarginine dimethylaminohydrolase (DDAH) in a rat model of sleeping sickness. PLoS One 2011;6:e16891.
19. Aribas A, Kayrak M, Tekinalp M, Akilli H, Alibasic H, Yildirim S, *et al.* The relationship between serum asymmetric dimethylarginine levels and subjective sleep quality in normotensive patients with type 2 diabetes mellitus. Korean J Intern Med 2015;30:316-24.
20. Xiao HB, Wang YS, Luo ZF, Lu XY. SZSJ protects against insomnia by a decrease in ADMA level and an improvement in DDAH production in sleep-deprived rats. Life Sci 2018;209:97-102.
21. Wang L, Liu W, He X, Chen Y, Lu J, Liu K, *et al.* Association of overweight and obesity with patient mortality after acute myocardial infarction: A meta-analysis of prospective studies. Int J Obes 2016;40:220-8.
22. Borgeraas H, Hertel JK, Svingen GFT, Pedersen ER, Seifert R, Nygård O, *et al.* Association between body mass index, asymmetric dimethylarginine and risk of cardiovascular events and mortality in norwegian patients with suspected stable angina pectoris. PLoS One 2016;11:e0152029.
23. Aeberli I, Gerber PA, Hochuli M, Kohler S, Haile SR, Gouni-Berthold I, *et al.* Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: A randomized controlled trial. Am J Clin Nutr 2011;94:479-85.
24. Zhu J, Su X, Li G, Chen J, Tang B, Yang Y. The incidence of acute myocardial infarction in relation to overweight and obesity: A meta-analysis. Arch Med Sci 2014;10:855-62.