

# The effect of pomegranate juice, lemon juice and secanjabin in reducing infra-cardiac activity of $^{99m}\text{Tc}$ -MIBI during myocardial perfusion imaging in comparison with fatty food

Mahdi Haghhighatafshar<sup>1</sup>, Ali Sarfaraz<sup>1</sup>, Aida Banani<sup>1,2</sup>,  
Farinaz Farhoudi<sup>3,4</sup>, Zahra Etemadi<sup>1</sup>

<sup>1</sup>Nuclear Medicine and Molecular Imaging Research Center, Namazi Teaching Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup>Department of Nuclear Engineering, Faculty of Advanced Sciences and Technologies, University of Isfahan, Isfahan, Iran

<sup>3</sup>Department of Persian medicine, Faculty of Medical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

(Received 13 January 2019, Revised 23 April 2019, Accepted 26 April 2019)

## ABSTRACT

**Introduction:** Eating fatty food is a common technique for decreasing extra cardiac activity, but sometimes patients refuse to eat fatty foods due to various reasons during myocardial perfusion imaging. The aim of this study is to introduce an alternative method for patients who are not able to use fatty foods to accelerate the transit of radiotracer from the liver.

**Methods:** A total of 100 patients were randomized into four groups to take 200 cc of lemon juice, 200 cc of pomegranate juice, 200 cc of secanjabin, and 100 mg of fatty meal, 10 min after injection of 20 mCi  $^{99m}\text{Tc}$ -MIBI, respectively in groups A, B, C, and D. The study is carried out in both rest and stress imaging at 30 and 50 min post-injection. Using ROI-based analysis, means of activity counts in heart and liver and, then the mean of heart/liver (H/L) ratios were calculated.

**Results:** According to data analysis of both rest and stress imaging at min 30 and 50, A and D groups had significantly higher H/L ratio than groups B and C. Comparing the images of groups in both rest and stress protocol at minutes 30 and 50, A and D groups had significantly higher H/L ratio at 50 minutes in comparison with 30 minutes.

**Conclusion:** In patients who refrain from eating fatty foods, drinking of diluted lemon juice may be recommended as a simple technique and the best alternative to decrease extra-cardiac activity and increase the H/L ratio.

**Key words:** Lemon juice; Fatty food; Infra-cardiac activity; Myocardial perfusion imaging; Sub-diaphragmatic activity

Iran J Nucl Med 2019;27(2):113-117

Published: July, 2019

<http://irjnm.tums.ac.ir>

**Corresponding author:** Zahra Etemadi, Nuclear Medicine and Molecular Imaging Research Center, Namazi Teaching Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. E-mail: [zahra.etemadi@gmail.com](mailto:zahra.etemadi@gmail.com)

## INTRODUCTION

Gated myocardial perfusion single photon emission computed tomography (Gated SPECT) is a non-invasive technique for evaluation of coronary artery disease (CAD), therapy planning, and risk stratification [1-3]. Radiotracers such as  $^{99m}\text{Tc}$ -hexakis-2-methoxyisobutylisonitrile ( $^{99m}\text{Tc}$ -MIBI) used in myocardial perfusion SPECT imaging are cleared by the liver and excreted into the bile, and passed into the intestinal lumen [4, 5]. Because of overlapping of heart with liver and bowel, occurrence of the scattered photons during the myocardial image acquisition is a routine and important phenomenon [6, 7]. Reviewing cine display of planar projections is necessary for checking quality of the imaging, sub-diaphragmatic activity, motion artifact and incidental findings [8]. In the reconstruction process of myocardial perfusion SPECT images using analytical or iterative algorithms, the projection bins affected by the scatter photons introduce an over or underestimation of radiotracer concentration in myocardium images, especially in the case of inferior wall [9, 10].

So far, several methods have been proposed for reducing adjacent cardiac activity and the impacts arising from it [11-22]. Generally, these methods can be classified into two categories: first, the imaging technical approaches including the implementation of attenuation correction method during the reconstruction [20] and second, oral consumption of various materials such as fatty meals [19], milk [11, 19, 21], milk and water [11, 12, 16, 22], water [13], sandwiches [18], lemon juice [15, 21, 22] or intravenous administration of a drug such as metoclopramide [17]. Different results have been demonstrated by these studies and still there is no established methodology, hence it appears is important to find a way to reduce intrusive activity of liver to improve the quality of myocardial perfusion images.

The aim of this study is to introduce an alternative method for patients who are not able to use fatty foods to accelerate the transit of  $^{99m}\text{Tc}$ -MIBI from liver, to this end, we compared four different materials including lemon juice, pomegranate juice, secanjabin (a solution made by mixing vinegar, sugar and mint) and fatty meal as a gold standard.

## METHODS

This study was performed prospectively as a randomized clinical trial registered in the Iranian registry of clinical trials (Id: 16196). This study has been approved by the Ethics Committee and Institutional Review Board of Shiraz University of medical sciences and the informed consent form were signed by all of the patients included in the study (Study Code No. 1392-01-01-6518).

## Study population

In an outpatient setting, this prospective, randomized, controlled trial comprised 100 patients who were referred to our nuclear medicine department for myocardial perfusion imaging. With a simple random sampling method, subjects were randomized to four groups of 25 patients in each group. Group A stands for using diluted lemon juice, group B for pomegranate juice, group C for secanjabin (a solution made by mixing vinegar, sugar and mint) and group D for fatty meal. All patients met the following criteria: no liver or biliary system disease, no previous cholecystectomy and no peptic ulcer within the last 6 months. Patients with a history of diabetes, previous myocardial infarction within the last 3 months, severe primary valvular disease, unstable angina, primary cardiomegaly, left ventricle hypertrophy, severe obstructive pulmonary disease or asthma were also excluded from the study.

## Patient preparation

Patients fasted for at least 4 hr before the pharmacological stress. Consumption of nitrates, caffeine containing foods or drugs and long acting aminophylline were held from 24 hr before the dipyridamole stress test.

## Protocol

A commercial MIBI kit (AEOI, Tehran, Iran) was used and the labeling and quality control procedures were performed according to the manufacturer's instructions.

The groups underwent a  $^{99m}\text{Tc}$ -MIBI SPECT imaging for two days rest-stress protocol. The subjects were induced a stress within 4 min intravenous injection of 0.56 mg/kg of dipyridamole. Then, they were injected with 20 mci of  $^{99m}\text{Tc}$ -MIBI and 10 min after injection, instructed to use 200 cc of diluted lemon juice (150 ml juice + 100 ml water; pH = 2.0), 200 cc of pomegranate juice (nutrient content per 240 ml was: total fat, 0 g; protein, 1 g; carbohydrate, 33 g; sodium, 36 mg ; potassium, 480 mg; vitamin C, 80% and calcium, 2%), 200 cc of secanjabin (a solution made by mixing vinegar, sugar and mint) and 100 g of cream as fatty food (nutrient content per 100 ml was: total fat, 30 g; protein, 2.9 g; carbohydrate, 3.3 g; phosphorus, 0.12 g ; and calcium, 0.1 g), respectively in A, B, C, and D groups. Myocardial perfusion imaging were performed at 30 and 50 min after injection of  $^{99m}\text{Tc}$ -MIBI at both rest and stress phases. Thereafter, there were four image series for each patient (rest imaging at 30 and 50 min and also stress imaging at 30 and 50 min).

Emission data were obtained using low-energy, high-resolution collimators by General Electric Infinia Hawkeye 4 scintillation dual-head gamma camera. By

setting an angle of 90° between two SPECT heads, and rotating them over 180° from the right anterior oblique 45° to left posterior oblique 45°, a step-and-shoot SPECT acquisition (totally 32 projection views) was performed with reconstruction matrix size of 64×64, zoom factor of 1.45, 30 second acquisition time per view, and 15% energy window set at 140 keV.

### Image analysis

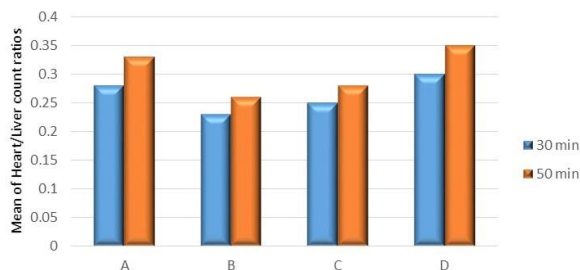
After acquisition, we drew the regions of interests (ROIs) in heart and liver regions on the rest and stress projections obtained at 30 and 50 minutes after radiotracer injection. The mean count in the ROI drawn on heart was divided to one in the ROI drawn on liver for each patient. The heart/liver (H/L) ratio can be used as an indicator for detecting interfering activity of the liver in myocardial SPECT images. The higher ratio confirms that the overestimation induced by interfering liver activity is decreased in myocardial SPECT projections.

### Statistical analysis

The results of the study were represented as the mean  $\pm$  standard deviation (SD) by using SPSS 18 and comparison between four groups was done with independence sample T-test and one-way ANOVA as well. A P-value of <0.05 was considered to indicate a statistically significant difference for all compared variables. On the basis of data provided by previous studies, the sample size of 25 patients in each of the four groups was estimated.

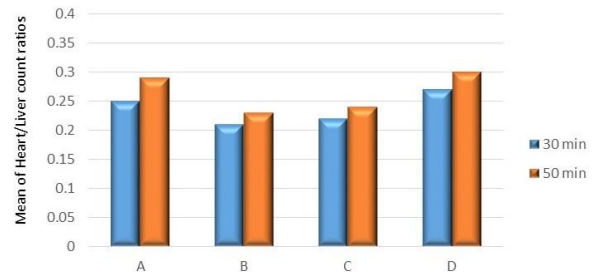
## RESULTS

According to data analysis of the rest imaging at min 30, A and D groups had significantly higher H/L ratio than groups B and C, but there was no significant difference between A and D groups (Table 1 and Figure 1). For the min 50 of the rest imaging, the same trend was observed (Table 1 and Figure 1).



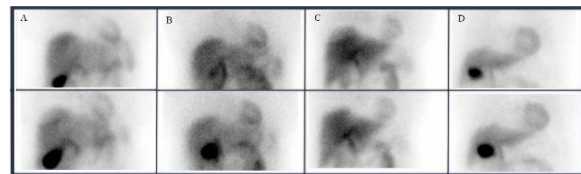
**Fig 1.** Mean of heart/liver count ratios in the groups A, B, C, D given lemon juice, pomegranate juice, secanjabin and fatty meal, respectively, obtained at 30 and 50 min at rest phase.

Also at min 30 of the stress imaging, A and D groups had significantly higher H/L ratio than groups B and C, but there was no significant difference between A and D groups (Table 1 and Figure 2). For the min 50 of the stress imaging, the same trend was observed (Table 1 and Figure 2).



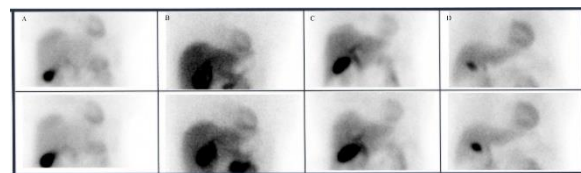
**Fig 2.** Mean of heart/liver count ratios in the groups A, B, C, D given lemon juice, pomegranate juice, secanjabin and fatty meal, respectively, obtained at 30 and 50 min at stress phase.

Comparing the images of groups in the rest protocol at minutes 30 and 50, A and D groups had significantly higher H/L ratio at 50 minutes in comparison with 30 minutes but there was no significant difference between minutes 30 and 50 in B and C groups (Figure 3).



**Fig 3.** A patient's planar imaging in each group obtained at 30 min (upper row) and at 50 min (lower row) after radiotracer injection at rest.

Comparing the images of groups in the stress protocol at minutes 30 and 50, the same trend were observed (Figure 4).



**Figure 4.** The same patient's planar imaging in each group obtained at 30 min (upper row) and at 50 min (lower row) after radiotracer injection at stress.

## DISCUSSION

According to the findings of this study consumption of fatty meal and lemon juice can be considered as effective ways to reduce interfering activity of the

**Table1:** Mean of Heart/Liver (H/L) count ratios calculated for the groups A, B, C, D given lemon juice, pomegranate juice, secanjabin and fatty meal, respectively, obtained at 30 and 50 min at rest and stress phase.

		A	B	C	D	p-value
Rest	30 min	0.28 ± 0.09	0.23 ± 0.05	0.25 ± 0.09	0.30 ± 0.03	0.013*
	50 min	0.33 ± 0.09	0.26 ± 0.06	0.28 ± 0.12	0.35 ± 0.02	0.002*
	p-value	0.04	0.05	0.16	<0.001	
Stress	30 min	0.25 ± 0.06	0.21 ± 0.06	0.22 ± 0.07	0.27 ± 0.03	0.004*
	50 min	0.29 ± 0.07	0.23 ± 0.07	0.24 ± 0.08	0.30 ± 0.04	0.003*
	p-value	0.03	0.12	0.12	0.004	

\*H/L ratios of A and D groups are significantly higher than B and C groups but there is no significant difference between A and D groups.

liver, but using secanjabin and pomegranate juice in spite of reducing interfering activity of the liver in some images does not have significant effect in comparison with fatty meal and lemon juice.

Iqbal et al. [13] showed that interpretation of inferoposteroseptal wall activity on myocardial rest SPECT images is facilitated by having the patient drink both whole milk and water at specified times before data acquisition, they indicated that Lipid-rich foods in the duodenum enhance the secretion of CCK, accelerating bile secretion and gallbladder emptying.

van Dongen et al. [12] evaluated 97 people and concluded that administration of both whole milk and water to patients at specified times, will improve the quality of attenuation-corrected myocardial perfusion SPECT images, thus facilitating the interpretation of the inferoposteroseptal myocardial wall.

Peace et al. [11] evaluated the effects of imaging time, radiopharmaceutical and full fat milk and water on the scattering from all extra-cardiac organs. The results demonstrated that delayed imaging may significantly improve the interpretation of images and in contrast with common practice, the administration of milk or water appears to be of no clinical value compared with delayed imaging. However, no significant difference in improving the image interpretation between  $^{99m}\text{Tc}$ -tetrofosmin and  $^{99m}\text{Tc}$ -MIBI was observed. Also, their quantitative findings revealed that the groups given milk or milk plus water showed no significant improvement against control groups.

Cherng et al. [15] showed that Drinking 250 ml diluted lemon juice 10 min after tetrofosmin injection on rest and stress MPI can improve image quality by accelerating tetrofosmin passage through the liver, and decreasing extra-cardiac, notably hepatic, interfering activities.

In this study we also found that consumption of lemon juice can be considered as an effective way to reduce interfering activity of the liver.

Lemon juice is rich in vitamin C, with a pH as low as 2.0. It is acidic enough to enhance bile secretion by

stimulating intestinal release of secretin. Unlike CCK, secretin significantly accelerates bile secretion, but plays little part in emptying the gallbladder. Therefore, the hepatic clearance of tetrofosmin is increased, but splanchnic activities are not enhanced by gallbladder emptying [15].

Malek et al. [22] examined three different drinks including water, milk, and lemon juice and concluded that drinking of 250 mL milk had significantly lowered interfering activity than other groups either in the rest or stress images.

Hence, the use of a method for improving the image quality had become a controversial issue.

According to the results of our study consumption of fatty meal and lemon juice, to some degree are proper techniques which can be used in myocardial perfusion imaging to reduce interfering activity of the liver. We also found that delayed imaging besides using fatty meal and lemon juice can improve the quality of images. A major limitation of our study is that the patients were not matched for gender and body mass indexes. Also visual assessment of extra cardiac activity was not done. Additionally, we did not compare the percentages of H/L ratios and interfering activities between different protocols within each patient.

## CONCLUSION

In patients who refrain from eating fatty foods, drinking of diluted lemon juice may be recommended as a simple technique and the best alternative to decrease extra-cardiac activity and increase the H/L ratio.

## Acknowledgments

This study has been part of a thesis (Ali Sarfaraz) and financially supported by Nuclear Medicine and Molecular Imaging Research Center, Shiraz University of Medical Sciences, Shiraz, Iran (grants No.6518). The authors would like to thank the staff of

nuclear medicine department of Namazi hospital for their cooperation. The authors wish to thank the Research Consultation Center (RCC) at Shiraz University of Medical Sciences for their invaluable assistance in editing this manuscript.

## REFERENCES

- Paul AK, Nabi HA. Gated myocardial perfusion SPECT: basic principles, technical aspects, and clinical applications. *J Nucl Med Technol.* 2004 Dec;32(4):179-87; quiz 188-9.
- Da Silva AJ, Tang HR, Wong KH, Wu MC, Dae MW, Hasegawa BH. Absolute quantification of regional myocardial uptake of <sup>99m</sup>Tc-sestamibi with SPECT: experimental validation in a porcine model. *J Nucl Med.* 2001 May;42(5):772-9.
- Fallahi B, Haghighatafshar M, Farhoudi F, Salehi Y, Aghahosseini F. Comparative evaluation of the diagnostic accuracy of <sup>99m</sup>Tc-sestamibi gated SPECT using five different sets of image acquisitions at stress and rest phases for the diagnosis of coronary artery disease. *Am J Nucl Med Mol Imaging.* 2014;4(1):10-16.
- Higley B, Smith FW, Smith T, Gemmell HG, Das Gupta P, Gvozdanovic DV, Graham D, Hinge D, Davidson J, Lahiri A. Technetium-99m-1,2-bis[bis(2-ethoxyethyl)phosphino]ethane: human biodistribution, dosimetry and safety of a new myocardial perfusion imaging agent. *J Nucl Med.* 1993 Jan;34(1):30-8.
- Wackers FJ, Berman DS, Maddahi J, Watson DD, Beller GA, Strauss HW, Boucher CA, Picard M, Holman BL, Fridrich R. Technetium-99m hexakis 2-methoxyisobutyl isonitrile: human biodistribution, dosimetry, safety, and preliminary comparison to thallium-201 for myocardial perfusion imaging. *J Nucl Med.* 1989 Mar;30(3):301-11.
- Monzen H, Hara M, Hirata M, Nakanishi A, Ogasawara M, Suzuki T, Sato T, Shimoyama H, Tadehara F, Hirose K, Yuki R. Exploring a technique for reducing the influence of scattered rays from surrounding organs to the heart during myocardial perfusion scintigraphy with technetium-99m sestamibi and technetium-99m tetrofosmin. *Ann Nucl Med.* 2006 Dec;20(10):705-10.
- Middleton GW, Williams JH. Interference from duodeno-gastric reflux of <sup>99m</sup>Tc radiopharmaceuticals in SPET myocardial perfusion imaging. *Nucl Med Commun.* 1996 Feb;17(2):114-8.
- Ghaedian T, Mortazavi S, Haghighatafshar M. Multiple myeloma and abdominal aortic aneurysm on myocardial perfusion raw images. *Clin Nucl Med.* 2015 Nov;40(11):e526-7.
- Heller EN, DeMan P, Liu YH, Dione DP, Zubal IG, Wackers FJ, Sinusas AJ. Extracardiac activity complicates quantitative cardiac SPECT imaging using a simultaneous transmission-emission approach. *J Nucl Med.* 1997 Dec;38(12):1882-90.
- Germano G, Chua T, Kiat H, Areeda JS, Berman DS. A quantitative phantom analysis of artifacts due to hepatic activity in technetium-99m myocardial perfusion SPECT studies. *J Nucl Med.* 1994 Feb;35(2):356-9.
- Peace RA, Lloyd JJ. The effect of imaging time, radiopharmaceutical, full fat milk and water on interfering extra-cardiac activity in myocardial perfusion single photon emission computed tomography. *Nucl Med Commun.* 2005 Jan;26(1):17-24.
- van Dongen AJ, van Rijk PP. Minimizing liver, bowel, and gastric activity in myocardial perfusion SPECT. *J Nucl Med.* 2000 Aug;41(8):1315-7.
- Iqbal SM, Khalil ME, Lone BA, Gorski R, Blum S, Heller EN. Simple techniques to reduce bowel activity in cardiac SPECT imaging. *Nucl Med Commun.* 2004 Apr;25(4):355-9.
- Hara M, Monzen H, Futai R, Inagaki K, Shimoyama H, Morikawa M, Tomioka N, Konishi T, Watanabe Y, Yuki R, Kobayashi H, Hirose K. Reduction of infracardiac intestinal activity by a small amount of soda water in technetium-99m tetrofosmin myocardial perfusion scintigraphy with adenosine stress. *J Nucl Cardiol.* 2008 Mar-Apr;15(2):241-5.
- Cherng SC, Chen YH, Lee MS, Yang SP, Huang WS, Cheng CY. Acceleration of hepatobiliary excretion by lemon juice on <sup>99m</sup>Tc-tetrofosmin cardiac SPECT. *Nucl Med Commun.* 2006 Nov;27(11):859-64.
- Rehm PK, Atkins FB, Ziessman HA, Green SE, Akin EA, Fox LM, Hixson DJ. Frequency of extra-cardiac activity and its effect on <sup>99m</sup>Tc-MIBI cardiac SPET interpretation. *Nucl Med Commun.* 1996 Oct;17(10):851-6.
- Weinmann P, Moretti JL. Metoclopramide has no effect on abdominal activity of sestamibi in myocardial SPET. *Nucl Med Commun.* 1999 Jul;20(7):623-5.
- Boz A, Gungor F, Karayalçin B, Yildiz A. The effects of solid food in prevention of intestinal activity in Tc-99m tetrofosmin myocardial perfusion scintigraphy. *J Nucl Cardiol.* 2003 Mar-Apr;10(2):161-7.
- Garcia EV, Cooke CD, Van Train KF, Folks R, Peifer J, DePuey EG, Maddahi J, Alazraki N, Galt J, Ezquerro N. Technical aspects of myocardial SPECT imaging with technetium-99m sestamibi. *Am J Cardiol.* 1990 Oct 16;66(13):23E-31E.
- Nuyts J, Dupont P, Van den Maegdenbergh V, Vleugels S, Suetens P, Mortelmans L. A study of the liver-heart artifact in emission tomography. *J Nucl Med.* 1995 Jan;36(1):133-9.
- Purbhoo K, Vangu MD. Efficacy of full-fat milk and diluted lemon juice in reducing infra-cardiac activity of (<sup>99m</sup>Tc) sestamibi during myocardial perfusion imaging. *Cardiovasc J Afr.* 2015 Jul-Aug;26(4):171-6.
- Malek H, Hedayati R, Yaghoobi N, Bitarafan-Rajabi A, Firoozabadi SH, Rastgou F. The effect of milk, water and lemon juice on various subdiaphragmatic activity-related artifacts in myocardial perfusion imaging. *Res Cardiovasc Med.* 2015 Sep 14;4(4):e29235.