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ORIGINAL ARTICLE

A randomized study of the effect of carbonated water prior to myocardial SPECT

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Abstract
Objective In myocardial perfusion single-photon emission computed tomography (SPECT), abdominal activity often interferes with the evaluation of perfusion in the inferior wall, especially after pharmacological stress. In this randomized study, we examined the effect of carbonated water intake versus still water intake on the quality of images obtained during myocardial perfusion images (MPI) studies.
Methods A total of 467 MIBI studies were randomized into a carbonated water group and a water group. The presence of intestinal activity adjacent to the inferior wall was evaluated by two observers. Furthermore, a semi-quantitative analysis was performed in the adenosine subgroup, using a count ratio of the inferior myocardial wall and adjacent abdominal activity.
Results The need for repeated SPECT in the adenosine studies was 5.3 % in the carbonated water group versus 19.4 % in the still water group ($p = 0.019$). The inferior wall-to-abdomen count ratio was significantly higher in the carbonated water group compared to the still water group (2.11 ± 1.00 vs. 1.72 ± 0.73, $p < 0.001$). The effect of carbonated water during rest and after exercise was not significant.
Conclusions This randomized study showed that carbonated water significantly reduced the interference of extra-cardiac activity in adenosine SPECT MPI.

Keywords Extra-cardiac radioactivity · Myocardial SPECT · Image quality enhancement · Carbonated water

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Introduction

Gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is widely used for the detection of myocardial ischemia and for obtaining additional prognostic information. Unfortunately, technical artifacts that occur during myocardial perfusion SPECT affect image quality. Abdominal tracer accumulation in the intestines and liver may lead to a falsely increased count density in the nearby cardiac wall. Furthermore, an active nearby extra-cardiac structure, e.g., the bowel, may cause a falsely decreased count density in the adjacent myocardial wall because of the effect of filtered back projection. The differences in abdominal activity on SPECT imaging between stress and rest conditions may mimic ischemia, especially in the inferior wall, and thereby potentially decreasing the diagnostic accuracy of the myocardial SPECT studies.

In daily practice, because of interference from the abdominal activity, repeat SPECT imaging needs to be performed in some patients, requiring more camera time. Alternatively, several techniques have been studied to improve myocardial SPECT quality, including the intake of water [1], milk [2], iodinated oral contrast [3] or lemon juice [4], all of which reducing interfering abdominal

activity, either by increasing the stomach volume or by accelerating the transit time of the tracer in the liver.

Hara et al. [5] showed another approach to increase stomach volume using carbon dioxide gas in patients undergoing pharmacological stress (adenosine). In the present randomized study, we compared the effects of carbonated water, which releases carbon dioxide gas, with those of still water in patients scheduled to undergo exercise myocardial SPECT, adenosine myocardial SPECT and rest myocardial SPECT.

Methods

Study population

The study included 141 adenosine stress tests (mean age patients 65 ± 11 year, 56 men), 105 exercise stress tests (mean age 59 ± 11 year, 57 men) and 216 rest studies (mean age 62 ± 12 year, 123 men). Patients were referred for a 2-day rest/stress Technetium-99m sestamibi (^{99m}Tc-MIBI) SPECT MPI between December 2009 and May 2010 at the Institute Verbeeten in Tilburg, the Netherlands. Patients were randomized into either a carbonated water (Spa Barisart, Spadel, Belgium) ($n = 233$) SPECT study group or still water (Spa Reine, Spadel, Belgium) ($n = 228$) group. The clinical characteristics of patients are listed in Tables 1, 2 and 3. The local ethics committee approved this study, and all patients gave written informed consent.

Table 1 The clinical characteristics of patients in the adenosine studies

Adenosine	Carbonated water group ($n = 76$)	Still water group ($n = 67$)
Age (year, mean ± SD)	64.5 ± 10.8	63.8 ± 11.5
Sex (male/female)	34/41	34/31
BMI (kg/m^2)	26.4 ± 8.1	27.8 ± 4.9
Previous CAD	56 %	60 %
Previous PCI	15 %	27 %
Systemic hypertension	60 %	40 %
Diabetes mellitus	24 %	23 %
Cigarette smoker	28 %	32 %
Nitrates	7 %	14 %
Beta-blockers	15 %	32 %
Calcium anatagonists	8 %	5 %

BMI body mass index, *CAD* coronary artery disease, *PCI* percutaneous coronary intervention, *SD* standard deviation

Myocardial perfusion SPECT (stress–rest 2-day protocol)

Patients were instructed to stop all relevant cardiac medication 24 h before stress testing and to have a light breakfast. Caffeine-containing beverages were withheld for 24 h prior to the test. An intravenous line of normal saline solution, with a 20-gauge cannula was positioned in an antecubital vein. Stress test was performed using pharmacologic agent adenosine or using exercise. Pharmacologic

Table 2 The clinical characteristics of patients in the exercise studies

Exercise	Carbonated water group ($n = 55$)	Still water group ($n = 51$)
Age (year, mean ± SD)	58.9 ± 12.8	59.5 ± 21.5
Sex (male/female)	36/19	21/29
BMI (kg/m^2)	26.0 ± 11.4	27.0 ± 4.6
Previous CAD	56 %	58 %
Previous PCI	22 %	20 %
Systemic hypertension	36 %	32 %
Diabetes mellitus	22 %	6 %
Cigarette smoker	27 %	24 %
Nitrates	13 %	6 %
Beta-blockers	25 %	34 %
Calcium antagonists	11 %	22 %

BMI body mass index, *SD* standard deviation, *CAD* coronary artery disease, *PCI* percutaneous coronary intervention

Table 3 The clinical characteristics of patients in the rest studies

Rest	Carbonated water group ($n = 115$)	Still water group ($n = 113$)
Age (year, mean ± SD)	61.4 ± 11.3	63.1 ± 12.5
Sex (male/female)	61/42	62/51
BMI	27.6 ± 11.3	26.9 ± 6.5
Previous CAD	64 %	53 %
Previous PCI	20 %	20 %
Systemic hypertension	52 %	41 %
Diabetes mellitus	23 %	20 %
Cigarette smoker	31 %	20 %
Nitrates	5.8 %	11.5 %
Beta-blockers	29.1 %	42.5 %
Calcium antagonists	8.7 %	7.9 %

BMI body mass index, *CAD* coronary artery disease, *PCI* percutaneous coronary intervention, *SD* standard deviation

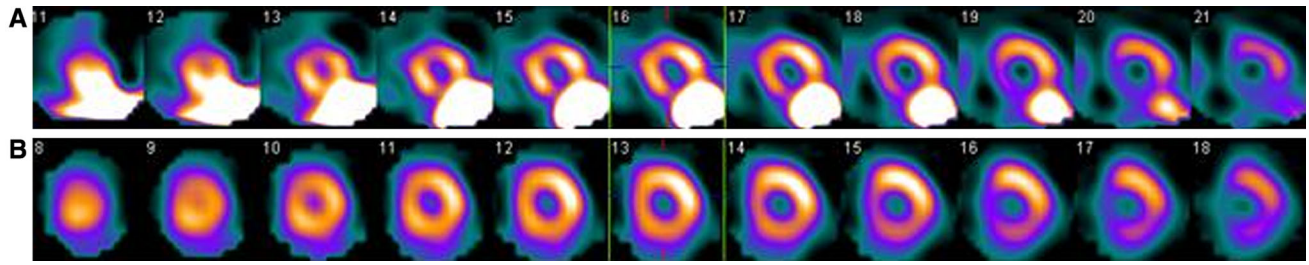

Fig. 1 **a** Adenosine stress SPECT shows interfering intestinal activity. **b** Repeated SPECT in the same patient shows normal MPI after ingestion of carbonated water and delayed imaging

vasodilatation was induced with intravenous administration of adenosine at a dose rate of 0.14 mg/kg/min for 6 min with standardized low level exercise.

The exercise was performed on a calibrated ergometer using a symptom-limited test with stepwise increased work. At maximum exercise, 375 MBq ^{99m}Tc-MIBI was injected. Peak exercise had to be continued for 1 min.

A 12-lead electrocardiogram and blood pressure were monitored throughout the stress study.

About 15 min after completion of the stress test, all patients ingested a drink of 250 ml (chocolate) milk and a cheese sandwich. Patients were randomized into a carbonated water group and a still water group. Just before the start of the image acquisition, all patients ingested 200 ml of water. The carbonated water (Spa Barisart, Spadel, Belgium) contains 6,400 mg/l CO_2, 5.5 mg/l calcium, 1.5 mg/l magnesium and 5 mg/l sodium.

SPECT imaging was performed 45 min after peak exercise radio tracer injection. Imaging was performed with a Siemens E.cam dual head variable-angle gamma camera. A low-energy high-resolution collimator was used. Electrocardiogram-gated myocardial SPECT acquisition protocol was performed post-stress. A symmetric 20 % window was centered at 140 keV, with a three-lead electric cardiographic monitoring. Imaging was acquired into a 64 × 64 computer matrix through a 180° rotation, with 32 positions with a 1.45 zoom; starting position is RAO 45°, with 8 frames per cycle. All studies were pre filtered using a backprojection. All images were subject to quality control measures, including patient motion correction, corrections for filed non-uniformity and center rotation. When automatic reconstruction or reorientation failed, reconstruction limits and axes were assigned manually. Visual analysis was performed on the myocardial perfusion data.

On day two, patients underwent a rest study. Acquisition parameters were identical to those of the stress study.

Two experienced physicians interpreted the SPECT results. The occurrence of abdominal activity adjacent to the inferior wall in all patients was determined visually. Patients had repeated SPECT after 45 min when the interfering activity could result in either important overestimation or underestimation of uptake in the myocardium, see Fig. 1. Consensus was obtained in cases of disagreement.

Quantification of inferior wall-to-abdomen count ratio

Quantification of the inferior wall-to-abdomen (I/A) count ratio was performed as described previously [5]. The ROI sizes were five pixels in diameter and were identical in every patient. Abdominal activity was measured, and ratios were calculated in a blinded manner. Physicians were also blinded with regard to the clinical characteristics of patients and the type of intervention.

Statistical analysis

Variables were contrasted between 2 groups of carbonated water and still water (control group) using a chi-square test. The I/A count ratios are expressed as mean ± SD and were compared with an unpaired student test (two-sided). A p value of less than 0.05 was considered to be significant.

Results

The need of repeated SPECT in the adenosine studies was 5.3 % in the carbonated water and 19.4 % in the still water group ($p = 0.019$), Fig. 2. Patients undergoing an exercise study were scheduled for a repeated SPECT scan in 3.6 % of the patients in the carbonated water group en 2.0 % of the patients in the still water group ($p = 0.59$), Fig. 3.

In the rest myocardial SPECT studies, 7.8 % of the patients in the carbonated water group needed a repeated SPECT against 4.4 % of the patients in the still water group ($p = 0.427$), Fig. 4.

For adenosine stress studies, the inferior wall-to-abdominal activity ratio was significantly higher in the carbonated water group than in the control group (2.11 ± 0.76 vs. 1.72 ± 0.50, $p < 0.001$) see Table 4.

The frequency of interfering intestinal activity on SPECT images in the control groups was significantly

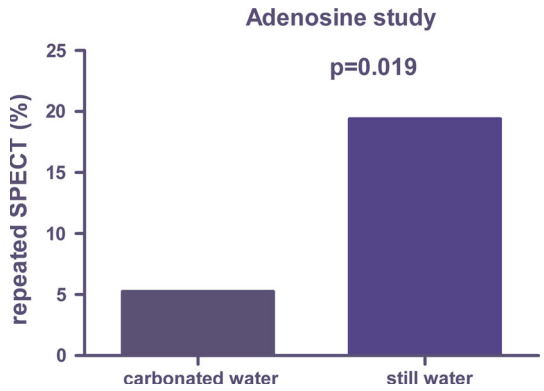

Fig. 2 Repeated SPECT scans using carbonated water versus still water in adenosine studies (%)

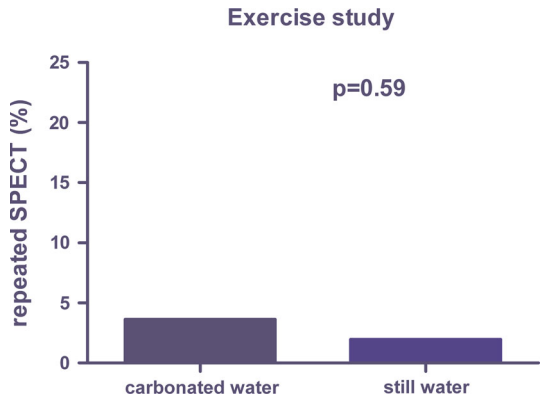

Fig. 3 Repeated SPECT scans using carbonated water versus still water in exercise studies (%)

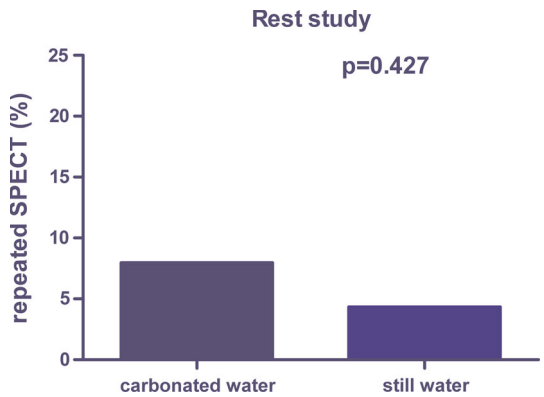

Fig. 4 Repeated SPECT scans using carbonated water versus still water in rest studies (%)

higher in the adenosine group compared to the exercise stress group (19.4 vs. 3.6 %, $p = 0.003$ chi-square 8.6) and to the rest group (19.4 vs. 4.4 %, $p = 0.001$ chi-square 11.3). The frequency of repeated SPECT scan was not significantly different between the exercise and rest studies ($p = 0.459$, chi-square = 0.548).

Table 4 Quantification of inferior wall-to-abdomen count ratio in adenosine studies

	Carbonated water group ($n = 76$)	Control group ($n = 67$)	p value
I/A (anterior)	2.02 ± 0.91	1.53 ± 0.65	<0.001
I/A (45° LAO)	2.34 ± 1.26	1.97 ± 0.80	<0.05
I/A (75° LAO)	1.96 ± 0.74	1.67 ± 0.67	<0.05
Mean value	2.11 ± 0.76	1.72 ± 0.50	0.001

All values are expressed as mean ± SD

I/A Inferior wall of myocardium-to-abdomen, *LAO* left anterior oblique

Discussion

The present study demonstrates that an intake of 200 ml carbonated water immediately before myocardial perfusion scintigraphy decreased abdominal activity adjacent to the inferior wall and improved the quality of adenosine ^{99m}Tc-MIBI myocardial perfusion SPECT images. Though, carbonated water did not improve the quality of the SPECT images in rest or during exercise, presumably because abdominal activity is a less frequent problem under these conditions.

A preceding study showed that carbonated water can improve myocardial SPECT image quality [5]. However, this observation was made only in patients under adenosine stress testing conditions. The present study extended these observations and compared the effects of carbonated water on the image quality in the adenosine stress SPECT, exercise stress SPECT and rest SPECT.

Previous studies showed two mechanisms underlying the reduction of abdominal activity due to water intake. First, water intake increases stomach volume, resulting in an increase in the distance between the heart and the intestine [6]. Carbon dioxide gas present in carbonated water may additionally enlarge the stomach and further increase the distance between the heart and the intestine, thereby reducing imaging artifacts. The 200 ml of carbonated water used in the present study can generate up to 650 ml of carbon dioxide gas, which expands the stomach considerably. Our findings are in accordance with the study by Hara et al. [5] who reported that the quality of the adenosine SPECT images was improved after consumption of 100 ml of carbonated water. We obtained a similar myocardial wall/abdominal ratio; hence, 100 ml of carbonated water may be sufficient to reduce interference from the abdominal activity. A reduction in the volume of ingested water may be helpful for patients with renal or cardiac failure; however, comparative studies with

different volumes of carbonated water are lacking. Furthermore, the study of Hara et al. included a control group without any fluid intake. Further studies are necessary to detect the effect of ingestion of small volumes of carbonated water upon image quality.

Not all patients consuming carbonated water showed an efficient reduction of the interference from abdominal tracer activity. This observation may be attributed to the transient effect of carbon dioxide on the stomach; therefore, the patients were asked to drink carbonated water immediately before imaging. Nonetheless, the effect of carbon dioxide decreases after eructation, which may explain the persistence of interfering abdominal activity in some patients who received carbonated water.

Another possible explanation for the improved image quality in adenosine stress SPECT studies due to carbonated water is the acidity of carbonated water, which has a pH of 4.05. In a study by Cherng, hepatobiliary excretion was found to be accelerated by diluted lemon juice [4]. In that study, the interference from intestinal activity after stress imaging was observed in 50 % of the patients who did not ingest any fluid ($n = 20$), 45 % of patients who ingested 250 ml water ($n = 20$), 40 % of patients who ingested 250 ml milk and only 10 % of patients who ingested 250 ml diluted lemon juice. The pH of the lemon juice was as low as 2.0, which is markedly lower than the pH of the carbonated water used in our study (pH = 4.05). Interestingly, another study in which patients received 250 ml lemon juice mixed with carbonated water improved the quality of myocardial perfusion scans of 33 patients [7]. The myocardium could be visualized more clearly; moreover, the scans showed an increased myocardial wall/abdominal ratio of 2.19 ± 0.71 with the lemon juice and carbonated water protocol, and this ratio is similar to the ratio obtained in our study (2.11 ± 0.76). Further studies are necessary to assess whether the addition of lemon juice to carbonated water is more effective than carbonated water alone. Although the exact pathophysiological mechanism underlying this effect remains unknown, the current study provides convincing evidence that carbonated water is more effective than still water in reducing the interference from abdominal activity in adenosine stress SPECT studies.

Exercise stress is the preferred modality for the induction of coronary hyperemia, because it allows a correlation between exertional symptoms and the perfusion pattern and provides information on exercise duration, workload achieved and the presence of ischemic ECG changes. Unfortunately, however, a substantial proportion of patients are incapable of attaining a sufficient level of exercise. With the introduction of dipyridamole and adenosine, those exercise-incapable patients can be tested using the coronary arteriolar vasodilator mechanism. Adenosine is a powerful, endogenous molecule that acts as a regulator of blood flow in many organ beds, including coronary circulation and the splanchnic bed. Adenosine causes a significant rise in splanchnic blood flow, whereas exercise decreases the splanchnic blood flow [8]. The different frequencies of interfering abdominal activity between adenosine and exercise protocols are probably secondary to the above mentioned differences in the splanchnic blood flow. Indeed, the interference of abdominal activity is less common after exercise than after vasodilator stress; in our study, only 2–3.6 % of patients required repeat imaging because of excessive abdominal activity after exercise. This low frequency of interfering abdominal activity after exercise may also explain the lack of effect of carbonated water in this patient group.

In conclusion, our results show that carbonated water improves adenosine myocardial perfusion SPECT imaging quality, thus reducing the need for repeated scanning. However, exercise remains the preferred stress modality because of the lower frequency of interfering abdominal activity in contrast to adenosine.

Conflict of interest The authors declare that they have no conflict of interest.

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