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ORIGINAL PAPER

Adenosine triphosphate (ATP) and adenosine cause similar vasodilator effect in patients undergoing stress perfusion cardiac magnetic resonance imaging

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Abstract
To evaluate the vasodilator effect of adenosine triphosphate (ATP) compared with adenosine in stress perfusion cardiac magnetic resonance (CMR) examinations. A total of thirty-three patients underwent clinically indicated stress/rest perfusion CMR examination following intravenous injection of a total dose of 0.2 mmol/kg of gadobutrol. Individuals were randomly assigned to ATP (160 mcg/kg/min) or adenosine (140 mcg/kg/min). The vasodilator effect of both drugs was analyzed by comparing differences in heart rate, symptoms during stress, and semiquantitative myocardial and splenic perfusion parameters, including time, time to peak, upslope, myocardial perfusion reserve index, tissue perfusion values, splenic and myocardial signal intensity ratios, and splenic-to-myocardial signal intensity ratios. No significant difference was found in heart rate variation between the stressors (26.1 ± 19.1 bpm for ATP vs. 21.7 ± 17.3 bpm for adenosine, p = 0.52). Patients receiving ATP referred less pronounced clinical symptoms. Semiquantitative myocardial perfusion parameters were comparable, and patients in the adenosine and ATP groups showed similar myocardial perfusion reserve index values (2.34 [1.62–2.73] vs 1.63 [1.29–2.10], p = 0.07). Splenic switch off was visually confirmed in all patients and estimated spleen to myocardium ratio was similar (0.92 [0.53–1.09] vs 0.81 [0.53–0.86] with ATP and adenosine, respectively, p = 0.12). Both ATP and adenosine are potent coronary vasodilators that can be safely employed in stress-CMR. Both stressor cause similar hyperemic response. Splenic switch-off can be used to assess stress adequacy in patients undergoing stress-CMR with either adenosine or ATP.

Keywords Heart · Myocardium · Adenosine · Adenosine triphosphate · Perfusion · Magnetic resonance imaging

Introduction

Most recent guidelines on myocardial revascularization recommend documentation of ischemia using functional non-invasive testing before elective invasive procedures in patients with suspected stable coronary artery disease [1]. Best-established stress-imaging techniques are echocardiography and myocardial perfusion scintigraphy, which can be performed in combination with exercise stress or pharmacological stress. More recently, vasodilator-induced stress cardiac magnetic resonance imaging (stress-CMR) has emerged as an alternative capable to provide an integrative assessment of cardiac structure and function. Further, this technique has become routine investigation for myocardial perfusion imaging in clinical practice [2].

For stress imaging, vasodilation is generally induced with either a continuous intravenous infusion of adenosine, or a bolus of intravenous dipyridamole or regadenoson [3]. Adenosine triphosphate disodium (ATP) is another vasodilator agent that has also been used for pharmacological stress myocardial perfusion imaging in the field of nuclear medicine [4]. This agent is a precursor to adenosine and it is expected to produce an equivalent hyperemic response [5, 6].

The diagnostic equivalence of an intravenous infusion of ATP vs. adenosine for myocardial perfusion imaging was demonstrated in a study performed using Thallium-201 myocardial tomography [7]. To our knowledge, the equality of

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ATP and adenosine in vasodilator-induced stress-CMR has not been established yet.

In this study, we sought to determine whether ATP and adenosine induce equivalent vasodilator stress by measuring semiquantitative myocardial perfusion parameters and the myocardial perfusion reserve index (MPRI). Further, we determined whether the recently described splenic switch-off sign that allows to demonstrate stress adequacy in adenosine stress CMR examinations could also be applied to ATP [8]. The side effects of both drugs were also compared. We hypothesized that if ATP proves to cause a similar vasodilator effect as adenosine in stress-CMR, this agent could also be employed in routine clinical examinations.

Materials and methods

Subjects

Thirty-three consecutive patients with suspected or known coronary artery disease underwent clinically indicated CMR examination with a conventional stress/rest perfusion protocol to rule out myocardial ischemia. All patients were in stable clinical condition and in sinus rhythm at the time of examination. Patients with classical contraindications for MRI, such as claustrophobia, pacemaker or automated implantable cardioverter-defibrillator (AICD) implantation, MR-unsafe objects, and chronic renal failure (glomerular filtration rate, GFR $\leq$ 30 ml/min) were excluded. Subjects were instructed to avoid caffeine-containing food and drinks 24 h prior to CMR examination.

The institutional review board approved the study protocol and informed consent was obtained from all individual participants included in the study.

CMR acquisition protocol

All stress-CMR examinations were performed on a 1.5 T system (MAGNETOM Aera, Siemens Healthcare GmbH, Erlangen, Germany). Standard steady-state free-precession (SSFP) cine images were acquired in the four-chamber, two-chamber and short-axis views to assess left-ventricular function.

For the vasodilator stress individuals were randomly assigned to intravenous ATP (15 patients) or adenosine (18 patients). All subjects had similar gender, age, weight and height (Table 1). ATP and adenosine were intravenously administered via right antecubital vein at 160 mcg/kg/min and at 140 mcg/kg/min for a minimum of 5 min and 3 min, respectively, and until an appropriate hemodynamic response was achieved (heart rate increase of at least 10 beats per minute).

Table 1 Demographics and clinical indications for stress-CMR in patients receiving ATP and adenosine

	ATP	Adenosine	p
Gender (male/female)	9/6	15/3	
Age (years)	64.3 ± 15.6	63.7 ± 10.4	0.53
Mean heart rate (bpm)	62.4 ± 11.5	65.5 ± 10.9	0.32
BSA (m^2)	1.8 ± 0.2	1.9 ± 0.2	0.17
LV-EF (%)	66.1 ± 6.9	60 ± 11.2	0.08
BSA indexed LV-EDV (mL/m^2)	78.6 ± 19.9	82.5 ± 25.4	0.63
BSA indexed LV-ESV (mL/m^2)	26.6 ± 9.2	35.5 ± 19.9	0.10
BSA indexed LV-mass (g/m^2)	72.5 ± 26.7	73.5 ± 13.9	0.89
Clinical indication for CMR			
Angina/atypical chest pain	7	12	
Cardiomyopathy	4	4	
Dyspnea	4	1	
Syncope	–	1	

bpm beats per minute, *BSA* body surface area, *LV* left ventricle, *EF* ejection fraction, *EDV* end-diastolic volume, *ESV* end-systolic volume

For stress perfusion intravenous contrast (gadobutrol, Gadovist, Bayer Schering Pharma AG, Berlin-Wedding, Germany) was administered at 0.1 mmol/kg followed by a 40 ml saline flush delivered by an automated dual-head injector (Medrad Inc, Warrendale, Pennsylvania, USA) at 4 ml/s. The same injection regime was repeated for rest perfusion 10 min later. A total Gadovist dose of 0.2 mmol/kg was administered. Perfusion exams were acquired with a fast low angle shot (FLASH) sequence at three slice locations (base, mid, and apex) every R-R interval for a period lasting 50 heartbeats, with the following parameters: repetition time/echo time 2.96/1.1 ms, 59 segments, voxel size 2.4 × 2.4 × 10 mm, field of view 380 × 285 mm, acquisition matrix 160 × 82, and slice thickness 10 mm.

Presence of delayed gadolinium enhancement was evaluated using a phase-sensitive inversion recovery (PSIR) sequence.

Analysis

Resulting CMR images were transferred to an external workstation equipped with cardiac post-processing software (Argus, Siemens Healthcare GmbH). Image analysis was blinded to the stress agent used.

The vasodilator effect of both drugs was clinically assessed by comparing differences in heart rate and symptoms during the stress.

Myocardial perfusion analysis

Analysis of left-ventricular volumes, function and mass was performed following the standardized methods. For the study

purpose, myocardial perfusion was semiquantitatively evaluated by manually tracing endocardial and epicardial contours by one observer in a mid-ventricular slice excluding the inner 10% and outer 30% of the myocardium [9]. The myocardium was divided into six equiangular segments. Left ventricular and myocardial signal intensity (SI) were determined for all time points. Time, time to peak, and the upslope of the resulting SI-time curves were obtained for each myocardial sector. Upslope values were corrected for the input function to compensate for the changes in compactness and velocity of the contrast agent bolus [10]. The MPRI was calculated by dividing the upslope results at maximal vasodilation through the results at rest [11].

Poor quality or incomplete studies and myocardial segments showing late gadolinium enhancement representing unknown prior myocardial infarction were excluded from the analysis.

Splenic switch-off

Splenic perfusion was visually and semiquantitatively analyzed by using SI curves after manual contouring of regions of interest in the septum myocardium and spleen on the stress and rest perfusion images of each patient. The peak signal intensity was regarded as tissue perfusion and estimated by subtracting the maximal SI after injection of contrast agent from the baseline SI [8]. Time to peak, SI values, tissue perfusion values, splenic and myocardial signal intensity ratios, and splenic-to-myocardial signal intensity ratios were calculated.

Statistical analysis

Data are presented as mean ± standard deviation or as median and interquartile range (IQR), as appropriate. Normal distribution of data was assessed with the Shapiro–Wilk test. Differences in left ventricular parameters were compared with independent samples t-test, whereas differences in myocardial perfusion values and semiquantitative splenic perfusion values between ATP and adenosine groups were compared with the nonparametric Mann–Whitney U test for independent samples. Intraindividual comparison of peak splenic SI and splenic time to peak values during stress and rest in ATP and adenosine groups was analyzed using the Wilcoxon signed rank test. All p values < 0.05 were considered statistically significant. Data analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp).

Results

Patient characteristics

All examinations were carried out without complications. No patient was excluded from participation. Patient characteristics and clinical indications for stress-CMR examinations are shown in Table 1. Most patients had at least one cardiovascular risk factor, such as hypertension, smoking history, hypercholesterolemia, diabetes mellitus, carbohydrate intolerance or obstructive sleep apnea syndrome. Stress-CMR examinations were performed in 19 patients with atypical chest pain, in 8 subjects with suspected cardiomyopathy, in 5 patients with dyspnea, and in 1 individual with syncopal episodes and family history of sudden cardiac death.

In both groups, most individuals were men. Clinical parameters did not statistically differ. Individuals in the ATP group had a mean age of 64.3 ± 15.6 years, a mean heart rate of 62.4 ± 11.5 beats per minute, a mean body surface area (BSA) of 1.8 ± 0.2 m^2, and left-ventricular mean ejection fraction (EF) of 66.1 ± 6.9%. Patients in the adenosine group had a mean age of 63.7 ± 10.4 years, a mean heart rate of 65.5 ± 10.9 beats per minute, a mean body surface area (BSA) of 1.9 ± 0.2 m^2, and left-ventricular mean ejection fraction (EF) of 60 ± 11.2%.

To achieve an appropriate hemodynamic response ATP and adenosine were administered for a mean time of 9.4 ± 6.1 min and 5 ± 2.7 min, respectively ($p = 0.016$).

There were no differences in the resting heart rate between groups (62.4 ± 11.5 bpm and 65.3 ± 10.7 bpm for ATP and adenosine, respectively, $p = 0.5$) and both vasodilators had a similar heart rate response (maximum heart rate of 79.5 ± 14.5 bpm for ATP vs. 79.2 ± 14.7 bpm for adenosine, $p = 0.95$). The increase in the heart rate between the stressors was also comparable (26.1 ± 19.1 bpm for ATP vs. 21.7 ± 17.3 bpm for adenosine, $p = 0.52$).

During pharmacologically induced stress, patients receiving ATP referred less pronounced clinical symptoms compared with those receiving adenosine. Symptoms were mild in 75% of patients in the ATP group whereas patients referred symptoms to be moderate in 40% of individuals receiving adenosine. Most frequently described side effect was chest pain in both groups (Table 2). Other reported clinical symptoms were flushing, dyspnea and headache. No myocardial infarction, bronchospasm, or atrioventricular block was observed.

Myocardial perfusion

A total of 193 myocardial segments were available for analysis. Five segments in 3 patients (2 in the ATP group and 1 in the adenosine group) were excluded from the analysis because of the presence of delayed gadolinium enhancement representing unknown prior myocardial infarction. No segments were excluded for poor image quality.

In all individuals, the stress-CMR examination was negative. No inducible ischemia was demonstrated. In all evaluated segments the MPRI was at least 1.5 [11].

Table 2 Frequency of clinical symptoms and adverse events associated with ATP and adenosine

Symptoms	ATP	Adenosine
No symptoms	5	2
Flushing	2	2
Dyspnea	1	3
Chest pain	7	11
Headache	1	0

In the ATP group 1 patient referred flushing and dyspnea. In the adenosine group 1 patient referred flushing and chest pain

Overall, there were not differences in semiquantitative myocardial perfusion measurements. Calculated time, time to peak (TTP) and upslope values during stress and rest did not differ in the ATP and adenosine groups (Table 3). Similarly, the per-segment analysis showed no differences in the semiquantitative myocardial perfusion parameters measured with ATP with respect to adenosine during stress and rest (Table 4). Overall MPRI values between the adenosine group 2.34 (1.62–2.73) and the ATP group 1.63 (1.29–2.10) were comparable (p = 0.07) (Table 5).

Splenic switch-off

Splenic switch-off was visually present in all ATP and adenosine stress-CMR examinations. This observation was confirmed after semiquantitative measurements of splenic perfusion parameters (Fig. 1).

Peak splenic SI markedly decreased in stress images as compared with rest images in both ATP (111.8 [59.9–125] vs. 138.3 [110.9–190], p = 0.035) and adenosine (118.9 [101.5-146.3] vs. 133.9 [119-211.5], p < 0.01) groups. Also, splenic time to peak differed between stress and rest images in patients undergoing stress-CMR with ATP (43 [34–49] vs. 35 [31–44], p = 0.02) and adenosine (41 [29–45] vs. 35 [27–42], p = 0.03).

Regarding splenic perfusion parameters, no significant differences were observed between the groups. Splenic tissue perfusion (96 [79-120.1] for ATP vs. 84 [68.6–95.3] for adenosine, p = 0.08) and splenic stress-to-rest signal intensity ratios (0.87 [0.68–1.01] for ATP vs. 0.77 [0.56–0.90] for adenosine, p = 0.27) were similar. Further, splenic-to-myocardial signal intensity ratios were comparable (0.92 [0.53–1.09] for ATP vs. 0.81 [0.53–0.86] for adenosine, p = 0.12).

Discussion

The main finding of this study is that both ATP and adenosine are potent vasodilators that can be safely employed in stress perfusion CMR. Further, the vasodilator effect of adenosine and ATP seems to be similar. We observed no significant differences in semiquantitative myocardial perfusion parameters and MPRI values between patients receiving adenosine with respect to those stressed with ATP (2.34 [1.62–2.73] vs 1.63 [1.29–2.10], p = 0.07).

ATP is a precursor to adenosine that is metabolized first into adenosine diphosphate, then into adenosine monophosphate, and finally into adenosine [12]. From the physiological perspective, the vasodilator mechanism of ATP is similar to that of adenosine, being the result of ATP binding to P2c -purinergic receptors and to adenosine A2A receptors [6]. Regarding the duration of the vasodilator effect, ATP possesses a slightly longer half-life than adenosine (20 s vs. 1 s) [5]. Also, the time required to achieve an appropriate hemodynamic response is longer with ATP than with adenosine, as confirmed in this study (9.4 ± 6.1 min vs. 5 ± 2.7 min, respectively, p = 0.016).

Studies performed in the field of nuclear medicine have established the role of ATP in the detection of coronary artery disease. In an investigation carried out to assess the diagnostic accuracy of ATP Thallium-201 myocardial perfusion imaging with respect to conventional coronary angiography, Miyagawa et al. observed sensitivity of 88% and specificity of 80% to detect CAD [7]. In a similar study, He et al. evaluated the feasibility, safety and diagnostic accuracy of pharmacologic stress with 99 m-Technetium-MIBI single-photon emission CT (99 m-Tc-MIBI-SPECT) using ATP in patients with suspected CAD [13]. These authors found sensitivity of 97% and specificity of 82% of ATP myocardial perfusion imaging compared with conventional coronary angiography, concluding that the former is a safe

Table 3 Overall comparison of semiquantitative measurements of myocardial perfusion in ATP and adenosine groups

	Stress			Rest		
	ATP	Adenosine	p	ATP	Adenosine	p
Time (s)	14.29 (13.27–17.99)	13.14 (11.08–18.04)	0.40	16.89 (15.29–20.09)	17.10 (15.88–20.05)	0.66
TTP (s)	11.20 (9.64–13.82)	9.71 (7.61–13.42)	0.18	15.78 (12.95–20.35)	15.07 (12.04–18.58)	0.44
Upslope (SI/s)	7.02 (5.48–10.58)	9.35 (6.30–13.98)	0.23	4.32 (3.42–5.58)	4.19 (2.73–5.05)	0.63

Data are presented as median (IQR). A p value < 0.05 was considered statistically significant

s seconds, *TTP* time to peak, *SI* signal intensity

Table 4 Per-segment comparison of semiquantitative measurements of myocardial perfusion in ATP and adenosine groups

	Segment 1						Segment 2					
	Stress			Rest			Stress			Rest		
	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p
Time (s)	14.57 (13.65–17.57)	13.01 (11.45–17.75)	0.29	16.36 (15.13–19.73)	16.49 (15.53–19.90)	0.88	14.29 (11.99–17.29)	13.01 (11.07–17.75)	0.448	15.67 (14.90–19.51)	16.37 (14.96–19.90)	0.80
TTP (s)	11.29 (9.08–14.01)	9.11 (7.38–13.32)	0.13	14.54 (12.76–17.90)	15.08 (12.29–18.50)	0.90	10.85 (9.60–14.01)	9.45 (7.26–13.30)	0. 15	15.61 (13.11–19.25)	13.80 (12.01–18.36)	0.33
Upslope (SI/s)	7.06 (4.31–10.24)	9.50 (6.49–14.31)	0.24	4.64 (3.61–5.42)	4.15 (3.09–5.14)	0.56	6.21 (4.85–10.02)	8.38 (5.50–13.26)	0.34	4.28 (2.43–5.55)	3.86 (2.87–5.05)	0.93
	Segment 3						Segment 4					
	Stress			Rest			Stress			Rest		
	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p
Time (s)	14.57 (14.25–18.04)	13.01 (11.28–18.38)	0.23	17.42 (15.63–19.63)	17.29 (16.05–19.62)	0.90	15.43 (14.25–18.04)	13.49 (11.48–18.10)	0.18	18.47 (16.05–20.90)	17.73 (16.28–21.09)	0.96
TTP (s)	11.55 (9.03–15.01)	9.11 (7.40–12.70)	0.20	14.41 (12.68–18.35)	14.94 (12.06–18.20)	0.66	11.30 (9.30–14.01)	10.65 (7.36–14.03)	0.40	15.86 (12.72–18.80)	15.14 (11.99–20.70)	0.93
Upslope (SI/s)	6.65 (5.29–9.35)	8.51 (6.04–12.09)	0.44	4.06 (3.30–6.08)	3.84 (2.87–5.33)	0.63	7.28 (4.17–11.29)	8.50 (5.81–13.38)	0.38	4.41 (3.05–6.05)	4.13 (2.40–4.86)	0.33
	Segment 5						Segment 6					
	Stress			Rest			Stress			Rest		
	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p	ATP	Adenosine	p
Time (s)	14.36 (11.79–17.57)	13.01 (11.02–18.10)	0.42	17.42 (14.97–20.40)	17.26 (16.09–18.28)	0.93	14.29 (11.79–17.44)	13.01 (11.02–17.32)	0.40	16.98 (14.90–19.73)	16.70 (15.87–19.65)	0.91
TTP (s)	10.18 (9.60–19.94)	9.70 (7.83–13.90)	0.24	15.56 (13.83–20.13)	13.94 (11.09–20.91)	0.40	11.67 (9.03–13.15)	9.74 (7.82–13.41)	0.27	15.15 (13.39–17.53)	15.60 (11.27–17.78)	0.61
Upslope (SI/s)	7.54 (4.34–11.44)	10.39 (6.33–14.56)	0.23	4.56 (2.87–5.41)	4.23 (3.01–5.21)	0.71	7.38 (6.50–11.24)	10.86 (6.75–14.98)	0.15	4.60 (3.57–5.11)	4.87 (2.87–5.53)	0.81

Data are presented as median (IQR). A p value < 0.05 was considered statistically significant

s seconds, *TTP* time to peak, *SI* signal intensity

Table 5 Overall and per-segment comparison of myocardial perfusion reserve indices (MPRI) in ATP and adenosine groups

	ATP	Adenosine	p
Overall	1.63 (1.29–2.10)	2.34 (1.62–2.73)	0.07
Segment 1	1.54 (1.19–1.96)	2.09 (1.78–2.95)	0.02*
Segment 2	1.69 (1.39–1.98)	2.09 (1.54–2.70)	0.18
Segment 3	1.73 (1.08–2.13)	2.08 (1.56–2.73)	0.13
Segment 4	1.48 (1.28–2.06)	2.33 (1.67–2.91)	0.08
Segment 5	2.01 (1.43–2.51)	2.11 (1.64–3.30)	0.13
Segment 6	1.72 (1.51–2.07)	2.41 (1.63–2.77)	0.1

Data are presented as median (IQR). A p value < 0.05 was considered statistically significant (*)

and feasible technique for detecting CAD in patients unable to perform the exercise test [13]. ATP myocardial perfusion imaging has also been shown to be useful for detecting potential ischemic areas that cannot be detected by exercise stress- myocardial perfusion imaging, particularly in patients with multi-vessel disease [14]. The experience of using ATP as stressor in CMR investigations, however, is scarce [15–18].

Compared to other stressors, one study showed that ATP stress ^{201}TI-SPECT is equivalent to dipyridamole stress ^{201}TI-SPECT in the detection of CAD [4]. In another study, Jeremias et al. [5] tested the equivalency of ATP to adenosine in their ability to cause maximal hyperemia as compared with the hyperemic response of complete coronary occlusion in six canines. These authors found that ATP was equivalent to adenosine for both Doppler derived coronary flow reserve (CFR) and pressure derived fractional flow reserve (FFR) [5]. Prior reports evaluated the potency of most widely employed vasodilator agents for stress perfusion CMR (adenosine, regadenoson and dypiridamole), demonstrating that regadenoson and adenosine, have similar vasodilator efficacy and are superior to dipyridamole [19]. To the best of our knowledge, this is the first study to directly compare the vasodilator properties of adenosine and ATP in routine clinical stress-CMR examinations. In all individuals, we observed that MPRI was at least 1.5, therefore indicating that vasodilator effect was achieved in all patients. Further, evaluated semiquantitative myocardial perfusion measurements and MPRI were comparable between the stressors.

Recently, the "splenic switch-off" phenomenon has also been reported as a tool to determine stress adequacy in myocardial adenosine perfusion MR imaging [8]. According to Manisty et al. failed splenic switch-off with adenosine allows to identify understressed patients who are at risk for false-negative findings on perfusion MR images [8]. In our study, the splenic switch-off was visually present in all ATP and

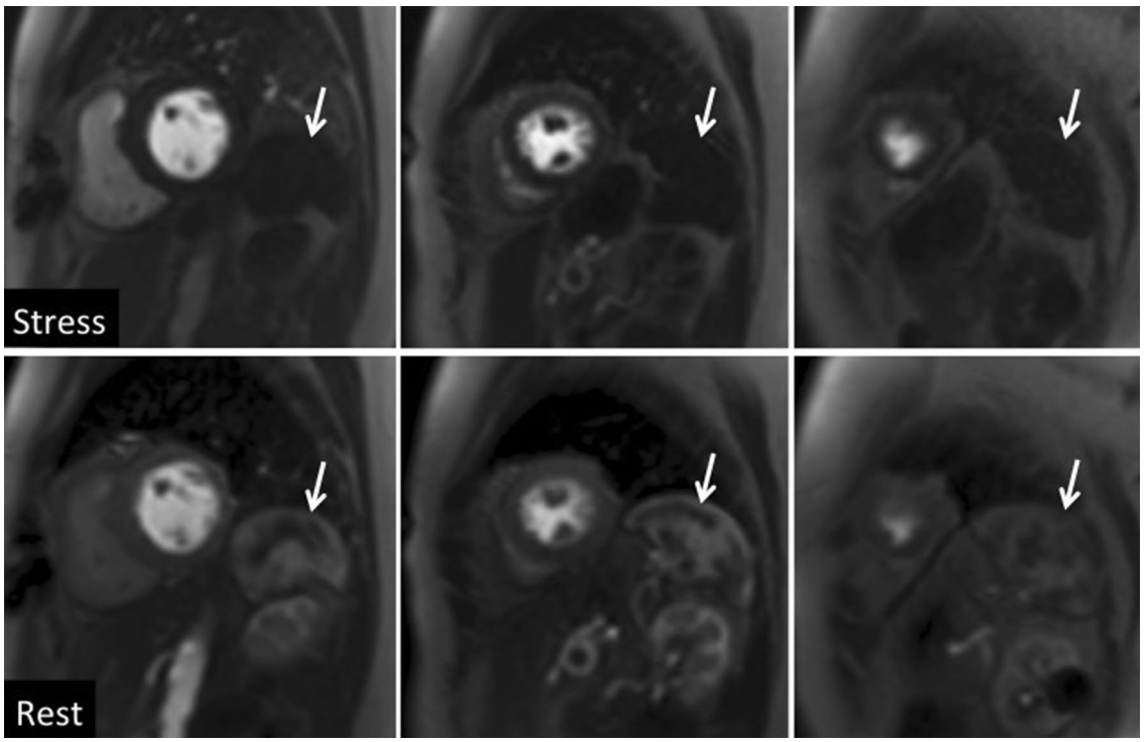

Fig. 1 Splenic perfusion MR images in a patient undergoing stress perfusion CMR with ATP. Images obtained at stress (upper row) and rest (lower row) demonstrate the splenic switch-off phenomenon (arrows), indicating stress adequacy

adenosine stress-CMR examinations. Further, semiquantitative measurements of splenic perfusion parameters in ATP and adenosine groups allowed objective assessment of this phenomenon. When differences between groups were compared, these were not significant. This result confirms that the splenic switch-off sign can also be employed to establish stress adequacy in myocardial ATP perfusion CMR.

From the clinical perspective, the two groups of patients showed a similar heart rate response to ATP and adenosine, although individuals receiving ATP required almost twice the time to achieve an appropriate hemodynamic response (9.4 ± 6.1 min vs. 5 ± 2.7 min), thus increasing the examination time. In our patient population ATP caused less pronounced clinical symptoms than adenosine, which is line with previously reported data [7]. Chest pain was referred by 67% of patients undergoing adenosine stress and by 47% of individuals receiving ATP. Interestingly, up to one-third of individuals receiving ATP remained asymptomatic during the examination. As described, no patient referred severe side effects, such as myocardial infarction, bronchospasm, or atrioventricular block.

This study is not without limitations. First, the evaluated cohort of patients available for the analysis was small and no power-analysis was performed. Second, direct comparison of the diagnostic accuracy of ATP and adenosine cannot be performed. Previous investigations have addressed this point and reported diagnostic equivalence of ATP and adenosine in the field of nuclear medicine [7]. In this study, we also confirm that semiquantitative myocardial perfusion measurements as measured by CMR (time, time to peak, upslope values, and MPRI) during stress and rest are similar. Finally, our investigation aimed at evaluating the vasodilator effect of ATP and adenosine in patients undergoing clinically indicated CMR investigations. In contrast to other studies designed to determine the relative potency of coronary vasodilators using healthy volunteers [19], we sought to include patients from our regular clinical practice so as to reproduce a routine clinical environment and a "real world" scenario.

In conclusion, ATP and adenosine are potent coronary vasodilators that can be safely used for stress perfusion CMR. ATP has a slower onset of action and causes mild side effects compared to adenosine, although it requires almost double administration time, slightly increasing study length. The hyperemic response to both stressors is similar. In patients undergoing adenosine or ATP stress perfusion CMR stress adequacy can be objectively demonstrated with the splenic switch-off phenomenon. Further research is warranted to establish the diagnostic accuracy of ATP in stress-CMR examinations.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this article. G. Bastarrika is speaker for General Electric and Siemens Healthineers and has received a research grant from Guerbet.

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