Clinical Research in Cardiology
https://doi.org/10.1007/s00392-026-02871-0

ORIGINAL PAPER

Safety and tolerability of pharmacologic stress with the selective A_{2A} adenosine receptor agonist regadenoson for the assessment of myocardial ischemia: results from 5780 consecutive patients in a cardiology practice

Sigmund Silber[1] · **Miriam Keller**[1] · **Manuela Rippel**[1]

Received: 25 October 2025 / Accepted: 3 February 2026

Abstract

Objectives This study investigated the safety and tolerability of regadenoson for pharmacologic stress testing in the context of myocardial scintigraphy under routine clinical conditions in a cardiology practice in 5780 consecutive patients.

Background The drug regadenoson was approved in Germany in 2010 for pharmacological stress testing in myocardial scintigraphy for patients who are unable to undergo adequate physical exercise. Previously, only dipyridamole or adenosine were available for diagnostic pharmacological vasodilation, but they were not approved for this indication.

Methods Data on safety and tolerability were prospectively collected from consecutive patients referred for the assessment of myocardial ischemia using myocardial scintigraphy. Data were immediately entered into a dedicated computer program.

Results After injection of regadenoson, there was a significant mean increase in heart rate from 70.2 ± 12.3 to a maximum of 94.6 ± 17.3 bpm. Systolic blood pressure dropped from 128.9 ± 16.2 to a minimum of 123.3 ± 20.3 mmHg. 86% of patients experienced any adverse effects, with the most frequent being dyspnea (64.2%), followed by headaches (20.7%), a sensation of warmth (20.2%), and numerous other, less frequent sensations. Bronchospasms were not observed, notably not in the 508 patients with COPD/ bronchial asthma. Asystole of > 6 s occurred in 2 patients (0.03%), which were both successfully terminated immediately with theophylline and atropine. There were no fatalities.

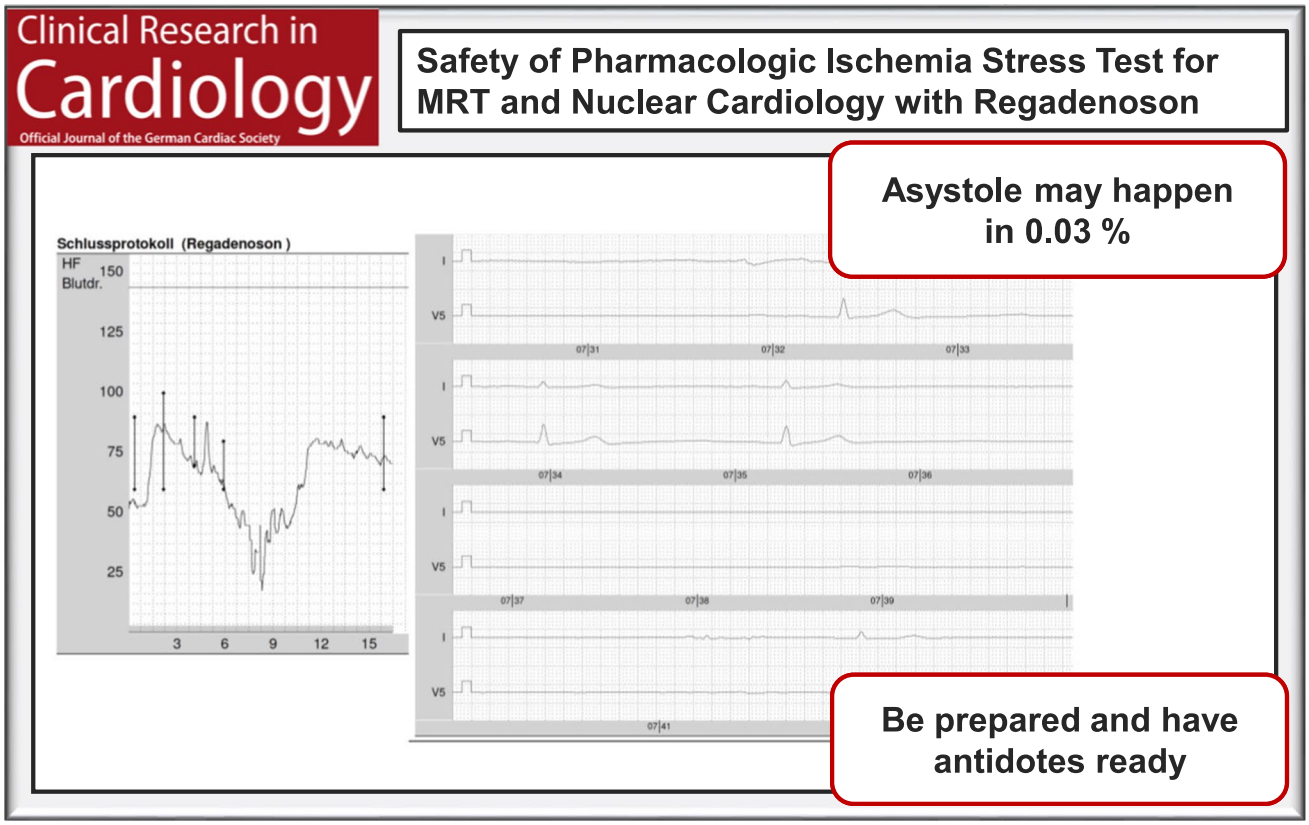
Conclusion Overall, regadenoson demonstrated very good tolerability. The development of the selective A_{2A} adenosine receptor agonist regadenoson, compared to classical non-selective adenosine, represents a significant advancement in non-invasive imaging diagnostics of myocardial ischemia, using myocardial scintigraphy and other modalities such as MRI. Since adenosine is contraindicated in patients with bronchial asthma/COPD, regadenoson has become the diagnostic agent of choice in these cases, although it must be considered that very rare instances ($< 0.1\%$) of life-threatening events can occur, necessitating that antidotes such as theophylline and atropine be readily available.

✉ Sigmund Silber
sigmund@silber.com

[1] Cardiology Center Munich, Tal 21, 80331 Munich, Germany

Published online: 09 March 2026

Graphical Abstract



Keywords Adenosine · Regadenoson · Myocardial ischemia · Stress imaging · Safety

Introduction

Chronic ischemic heart disease, today known as chronic coronary syndrome (CCS), remains the leading cause of death among both men and women also in Germany [1]. Thus, early detection continues to play a central role. Detection can occur either anatomically, through the imaging of coronary arteries, or functionally, via myocardial ischemia diagnostics. The traditional method of non-invasive ischemia diagnostics, the exercise ECG, due to its low sensitivity of 58% and specificity of 62% [2], is not recommended any more or only in exceptional circumstances (recommendation level IIb B) in the current guidelines of the European Society of Cardiology (ESC) but only if imaging methods for ischemia diagnostics are not available [3]. Nr. 3 must be labelled as a reference with the link. Since imaging ischemia diagnostics have a significantly higher diagnostic accuracy, they are clearly preferred (recommendation level I B) [3]. In daily practice, three imaging methods are considered: stress echocardiography, myocardial perfusion scintigraphy (SPECT), and magnetic resonance imaging (MRI). With an aging population and limited physical mobility, the likelihood of achieving meaningful physical stress decreases, thus increasing the necessity for pharmacologic stress testing. Furthermore, stress imaging with MRI can only be performed using pharmacological stress. According to ESC guidelines, the imaging method that is best available locally and with the greatest local expertise should be preferred (recommendation level I C) [3]. In our cardiology group practice, this is myocardial scintigraphy. For this purpose, both adenosine and regadenoson are available, which are equivalent in their vasodilating properties [4] and consequently in their diagnostic accuracy of ischemia [5–9]. Regadenoson was developed as a selective A_{2A} adenosine receptor agonist to substantially reduce the significant side-effect profile associated with adenosine. This is especially important for use in patients with bronchial asthma/COPD, in whom adenosine is contraindicated [10].

Due to the limited data and case reports available on the safety and tolerability of pharmacologic stress with regadenoson in the routine practice of a cardiology clinic,

we have documented and evaluated this in a prospective study in our practice.

Methods

Study population

The patient cohort was derived from existing clinic patients and referrals. Patients who, due to physical limitations, could not undergo significant physical stress testing were administered regadenoson for pharmacologic stress as part of SPECT ischemia diagnostics. From December 27, 2013, to July 30, 2018, regadenoson was administered to 5780 out of a total of 28,351 patients, which corresponds to 20.4% of the patient cohort. The mean age was 79.1 ± 9.7 years (range 33–95 years). There were 2576 male patients and 3204 female patients. A total of 395 patients (7%) had a prior diagnosis of COPD, and bronchial asthma was known in 113 patients (2%). A first-degree AV block (PQ time > 200 ms) was known in 1051 patients (18.2%).

Procedure

Patients provided written informed consent to anonymously use their data before the commencement of the test. They were instructed to fast for at least 3 h prior to the examination. To avoid potential interactions with regadenoson, patients were advised to abstain from xanthine-containing medications, as well as coffee, black or green tea, energy drinks, or cola beverages for 12 h beforehand. Regadenoson was administered in a standard dose of 400 µg. Shortly after the injection, typically with a noticeable increase in heart rate indicating the onset of action, 99 mTc-Tetrafosmin was administered (average dose approximately 250–300 MBq, weight-adjusted). During the imaging diagnostics using a double-head gamma camera, patients were positioned in a semi-reclining, relaxed posture to reduce possible artifacts of abdominal overlay. Heart rate was continuously monitored, and blood pressure and ECG were monitored at rest, and at 5 and 10 min post-injection. Any symptoms and potential complications were prospectively documented. In the event of severe complications, experienced personnel intervened and provided immediate medical management under the supervision of on-site physicians.

Documentation and statistics

Vital parameters and ECG changes recorded during the examination. Any occurring symptoms or complications were immediately first hand written documented on a prepared sheet of paper reflecting the identical fields of the computer program (Fig. 1). For each patient, one sheet of paper was used and later manually transferred to the database of the dedicated computer program (Filemaker Pro 16 Advanced®, Fig. 1). Data were analyzed using the Student's *t*-test as means with standard deviation.

Results

Heart rate before and after injection of regadenoson

There was a significant increase in heart rate among the majority of patients (Table 1). Following the administration of regadenoson, there was a maximum increase in heart rate of 24.4 bpm,

Blood pressure before and after injection of regadenoson

The majority of patients experienced a decrease in both systolic and, to a lesser extent, diastolic blood pressure following the injection of regadenoson (Table 2). The average baseline systolic blood pressure was 128.9 ± 16.2 mmHg. The minimum systolic value post-injection of the agent averaged 123.3 ± 20.3 mmHg. Overall, the systolic blood pressure remained 5 mmHg below the baseline systolic value 10 min post-injection.

Tolerability

Out of 5780 patients, 812 (14%) experienced no adverse effects, while the remaining 86% did.

Frequent adverse effects of regadenoson injection

Frequent adverse effects are defined as those occurring with a frequency in double-digit percentages. Overall, frequent side effects occurred in 69% of the patients with several side effects being present in the same patient (Table 3).

Rare adverse effects of regadenoson injection

Rare adverse effects are defined as those occurring in the single-digit percentage range. Overall, rare side effects occurred in 11% of the patients, with several side effects being present in the same patient (Table 4).

Serious complications

Overall, there were serious complications in 6 patients, evenly distributed at 0.03% each (Table 5). These included asystole lasting ≥ 6–10 s, which occurred in both cases in patients with previously known first-degree AV block, an

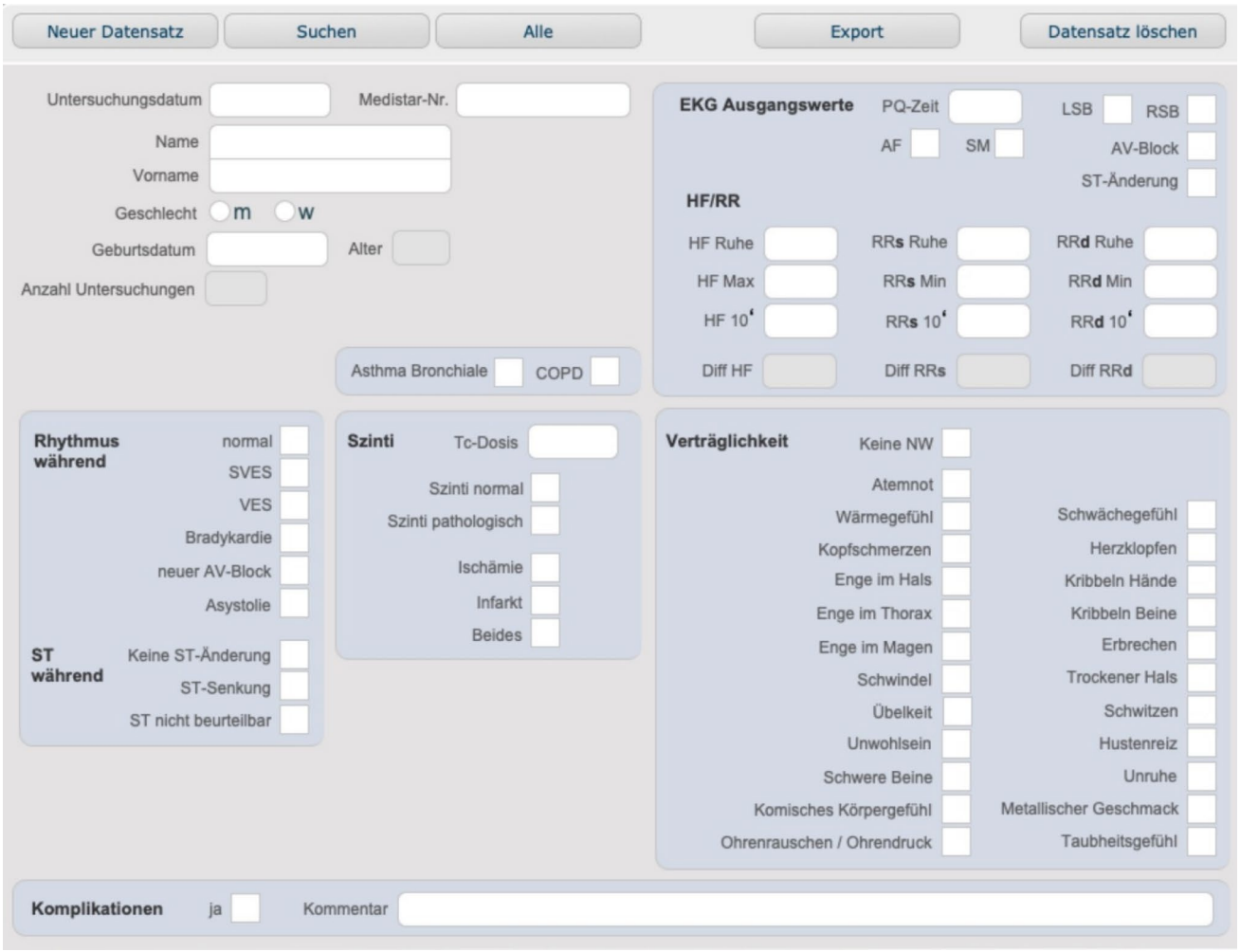


Fig. 1 Computer input screen for prospectively collected data using Filemaker Pro 16 Advanced®

Table 1 Heart rate before and after administration of regadenoson

Resting (baseline)	**70.2 ± 12.3 beats per minute**
Maximum	**94.6 ± 17.3* beats per minute (vs. rest)**
Change from baseline	+24.4 beats per minute
After 10 min	**79.4 ± 13.2* beats per minute (vs. rest)**
Change from maximum	−15.2 beats per minute
Change from baseline after 10 min	+9.2 beats per minute

*$p < 0.001$ according to Student's *t*-test

intermittent second or third-degree AV block with a pause lasting several seconds (Fig. 2), two patients with symptomatic bradycardia with a heart rate below 40 beats per minute, two patients with symptomatic decline in systolic blood pressure, and two patients with a cerebral seizure. All serious complications were observed within 10 min

Table 2 Heart rate before and after administration of regadenoson

Systolic blood pressure	
Resting (baseline)	**128.9 ± 16.2 mmHg**
Minimum	**123.3 ± 20.3 mmHg* (vs. baseline)**
Change from baseline	−5.6 mmHg
After 10 min	**123.9 ± 15.5 mmHg* (vs. baseline)**
Change from minimum	+0.6 mmHg
Change from baseline	−5 mmHg
Diastolic blood pressure	
Resting (baseline)	**73.7 ± 8.1 mmHg**
Minimum	**69.3 ± 9.0 mmHg* (vs. baseline)**
Change from baseline	−4.4 mmHg
After 10 min	**70.8 ± 8.0 mmHg* (vs. baseline)**
Change from minimum	+1.5 mmHg
Change from baseline	−2.9 mmHg

*$p < 0.001$ according to Student's *t*-test

Table 3 Frequent adverse effects of regadenoson

Adverse effects	Patient number	Percentage
Dyspnoea or "feeling of increased breathing effort"	3709	**64.2%**
Headaches	1199	**20.7%**
Sensation of warmth	1168	**20.2%**
Thoracic pressure	971	**16.8%**
Abdominal pressure	935	**16.2%**

Table 4 Rare adverse effects of regadenoson

Adverse effect	Patient number	Percentage
Dizziness	519	**9.0%**
Nausea	342	**5.9%**
Tingling in the legs	266	**4.6%**
Tightness in the throat	200	**3.5%**
Weakness	176	**3.0%**
Cough	173	**3.0%**
Throat or mouth dryness	116	**2.0%**
Tingling in the hands	99	**1.7%**
Palpitations	102	**1.7%**
Vomiting	39	**0.7%**
Sweating	43	**0.7%**

of the injection of regadenoson, and no serious complications occurred after 10 min. These severe and potentially life-threatening complications were immediately countered with intravenously administered theophylline (200 mg slow i.v.) and atropine (in 0.5 mg doses i.v.). No fatal complications occurred.

Discussion

Overall, regadenoson was found to be very well tolerated. Even the serious complications occurring at the per-mille level were promptly resolved with theophylline and atropine. No patient died in relation to the procedure. Similarly, a previous study involving 2104 patients reported no fatalities [11]. However, the risk of asystole must be considered, albeit rare, even in the absence of a pre-existing AV block [12–17]. In a large meta-analysis of 34 studies, adenosine was associated with a higher-grade AV block in 5.2% of 14,672 patients, whereas only 0.05% of 8285 patients experienced this under regadenoson [18]. Nitroglycerin should be avoided as a "countermeasure" for significant adverse effects [19]. Minor adverse effects might occasionally be mitigated with caffeine [20, 21]. The pre-administration of aminophylline has been suggested to reduce adverse effects [22], but we did not implement this as both caffeine and aminophylline can counteract the vasodilatory effects of regadenoson. Accordingly, we advise patients to refrain from consuming coffee before the examination and to discuss the use of "respiratory medications" with us in advance.

Among the group of patients with serious complications, there were no cases of bronchial asthma or COPD, and conversely, regadenoson did not induce bronchospasm in any patient in our series. Our findings are consistent with other studies where no clinically relevant decrease in FEV1 (Forced Expiratory Volume) was observed in patients with COPD [23–26] or bronchial asthma [24, 27]. Nevertheless, for safety, regadenoson should be administered with caution to patients with bronchial asthma, as smaller studies have occasionally described "shortness of breath" in this patient group [23, 24, 27].

Furthermore, there were no strokes induced by regadenoson in our series, although they have been observed rarely [28–30] and led to a warning in the form of a "Red Hand Letter" [31]. Additionally, the use of regadenoson is advised against in patients with known hemiplegic migraine [32]. In our study, all serious complications occurred within 10 min of injection, during the interval of strict observation. After this period, no complications arose, allowing the patients to be safely placed under the gamma camera.

Comparison of the mechanisms of action of regadenoson and adenosine

Regadenoson is considered as a clinically relevant improvement of adenosine [33–35]. The following Fig. 3 illustrates the basic mechanisms of action of the two agents. Adenosine

Table 5 Serious complications of regadenoson

Serious complications	Patient number	Percentage
Asystole (≥ 6 bis 10 s) (both patients exhibited a first-degree AV block in the baseline rhythm)	2	**0.03%**
Intermittent second- or third-degree AV block (with asystoles of 3 and 4 s, respectively)	2	**0.03%**
Symptomatic bradycardia (< 40 beats per minute)	2	**0.03%**
Symptomatic blood pressure drop (to approx. 60 mmHg)	2	**0.03%**
Cerebral seizure	2	**0.03%**

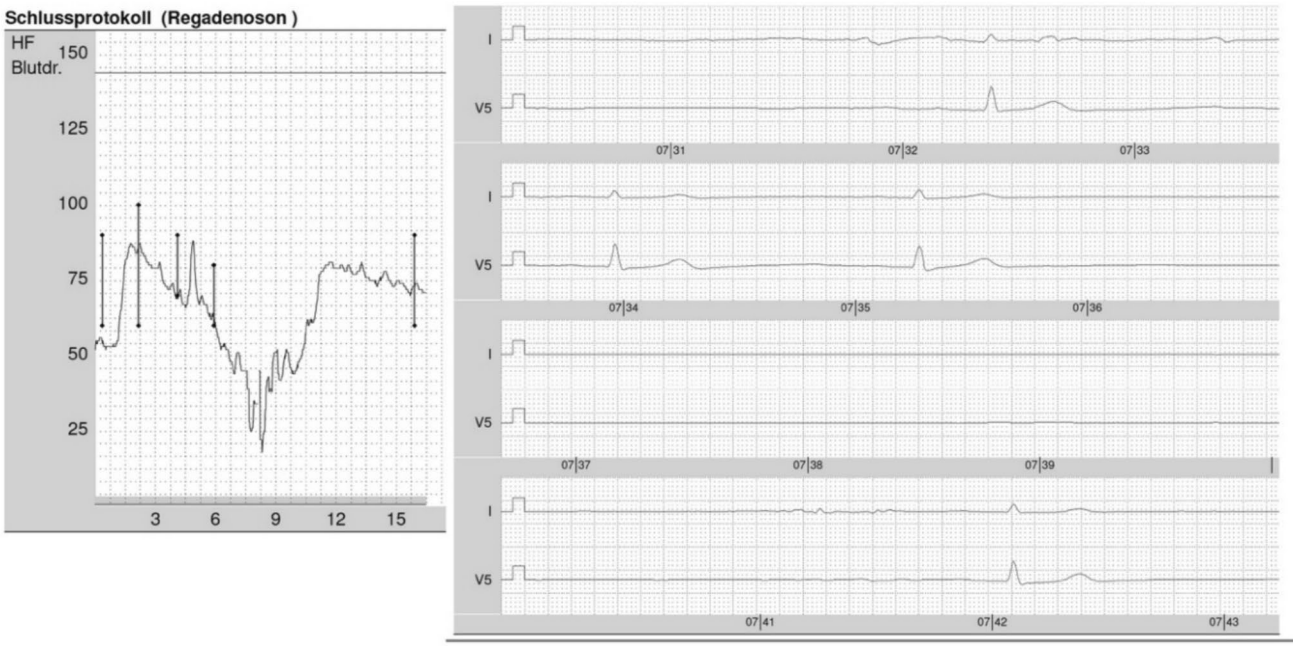


Fig. 2 Short-lasting asystole after injection of regadenoson, which was quickly resolved by administration of theophylline and atropine (see text)

acts directly (and the older agent dipyridamole indirectly) on the A_{2A} receptor. However, adenosine and dipyridamole are non-selective and also activate other adenosine receptor subtypes, leading to frequent clinically significant side effects (e.g., AV-block due to A1 activation and bronchoconstriction due to A_{2B} and A_3 receptor activation) as well as other less severe but often unpleasant side effects. In contrast, regadenoson selectively targets the A_{2A} receptors, thereby directly achieving the desired coronary dilation for ischemia diagnostics using SPECT and MRI, or fractional flow reserve (FFR), with fewer adverse effects compared to adenosine. In particular, our results confirm the postulated minimal or absent interaction with the A_{2B} and A_3 receptors. However, the AV-blocks we observed, albeit very rarely, suggest a still slight interaction with the A_1 receptor.

Ischemia diagnostics with adenosine

Adenosine non-selectively activates four receptor subtypes, namely A_1, A_{2A}, A_{2B}, and A_3 (see Fig. 3). Activation of the cardiac and peripheral A_{2A} and A_{2B} adenosine receptors thus causes dilation of the coronary and peripheral arterial vasculature and increases myocardial blood flow. However, the activation of cardiac A_1 receptors mediates negative chronotropic, dromotropic, inotropic, and anti-beta-adrenergic effects, which are undesired. Furthermore, stimulation of A_3 and A_{2B} receptors is responsible for triggering mast cell degranulation and bronchoconstriction [33]. The primary effect desired with adenosine in ischemia diagnostics is the increased myocardial blood flow, which is solely induced by stimulation of A_{2A} and A_{2B} receptors, although A_{2B} receptors unfortunately also contribute a bronchoconstrictive component.

The image quality of SPECT scans obtained under adenosine stress can be improved by adding a small ergometric load (20–40 W). The main advantage of this combination is reduced uptake of the radiopharmaceutical in the gastrointestinal tract [39].

Ischemia diagnostics with regadenoson

Regadenoson is a selective A_{2A} adenosine receptor agonist and offers a more favorable side-effect profile compared to adenosine [40, 41]. As a selective A_{2A} receptor agonist, regadenoson has a more than 13-fold lower affinity for the A_1 receptor than for the A_{2A} receptor [42]. This accounts for its lack of sensitivity and the reduced negative chronotropic and dromotropic effects compared to adenosine. It is administered as a single bolus injection, has a longer half-life, and achieves a similar peak hyperemic response compared to adenosine [43].

Regadenoson is marketed under the brand name Rapiscan® and has been approved in the EU since 2010. In Germany, the drug has been available since September 2011 and is a prescription medication. Initially, regadenoson was only approved for SPECT myocardial scintigraphy, and the S1 guideline of the German Society for Nuclear Medicine (DGN) cites improved visualization of perfusion in diagnostic myocardial perfusion SPECT as its indication [38]. In the years following, further approvals for other areas in coronary

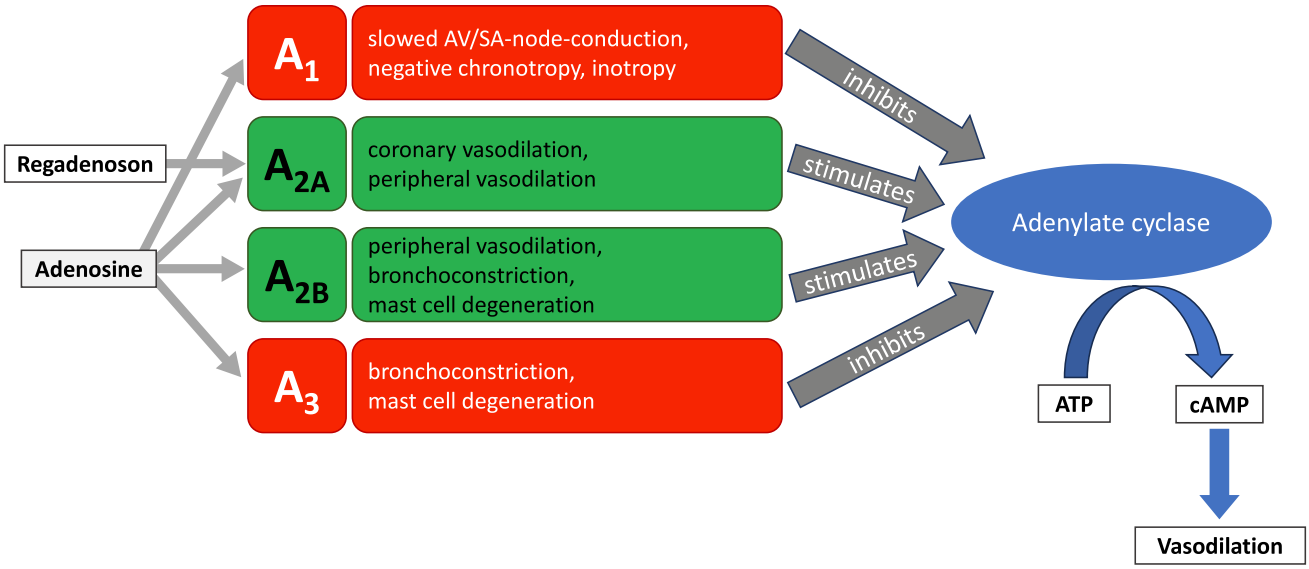


Fig.3 The different subtypes of adenosine receptors, their activating and inhibitory effects, and their differential stimulation by adenosine and regadenoson (modified according to reference[26])

heart disease (CHD) diagnostics have been granted, such as cardiac stress MRI and the invasive determination of fractional flow reserve (FFR). Particularly in stress MRI, regadenoson has rapidly become established, as—compared to adenosine—only one venous access is required instead of two [44, 45]. In contrast to adenosine, underlying diseases such as bronchial asthma or COPD are not contraindicated to the use of regadenoson.

The most frequent adverse effects of regadenoson described in the literature (in more than 10% of patients) include headaches, dizziness, flushing, dyspnea (breathing difficulties), gastrointestinal complaints, and chest pain [46–49]. Regadenoson should not be used in patients with bradycardia unless they have a pacemaker. Other contraindications include acute coronary syndrome, severe hypotension, or decompensated heart failure. Regardless, the outcome of the regadenoson-SPECT has significant prognostic significance [50, 51].

Conclusion

The development of the selective A_{2A} agonist regadenoson represents a significant advance over the traditional non-selective adenosine for pharmacological stress imaging. Since adenosine is contraindicated in patients with bronchial asthma or COPD, regadenoson is now the diagnostic agent of choice in these cases. Nevertheless, one should be aware that still life-threatening side effects can occur in less than one per mille. Therefore, the staff must be specifically trained and hold antidotes immediately ready for these possibly life-threatening events.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Statistical Office (2022) Causes of deaths in 2020. Wiesbaden, Germany. https://www.destatis.de. Accessed October 2025.
2. Knuuti J, Ballo H, Juarez-Orozco LE, Saraste A, Kolh P, Rutjes AWS, Juni P, Windecker S, Bax JJ, Wijns W (2018) The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. Eur Heart J 39:3322–3330
3. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJ, Group ESCSD (2020) 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 41:407–477
4. Vasu S, Bandettini WP, Hsu LY, Kellman P, Leung S, Mancini C, Shanbhag SM, Wilson J, Booker OJ, Arai AE (2013) Regadenoson and adenosine are equivalent vasodilators and are superior than dipyridamole- a study of first pass quantitative perfusion cardiovascular magnetic resonance. J Cardiovasc Magn Reson 15:85
5. Iskandrian AE, Bateman TM, Belardinelli L, Blackburn B, Cerqueira MD, Hendel RC, Lieu H, Mahmarian JJ, Olmsted A, Underwood SR, Vitola J, Wang W, Investigators AM (2007) Adenosine versus regadenoson comparative evaluation in

myocardial perfusion imaging: results of the ADVANCE phase 3 multicenter international trial. J Nucl Cardiol 14:645–658
6. Frey SM, Honegger U, Clerc OF, Caobelli F, Haaf P, Zellweger MJ (2022) Left ventricular ejection fraction, myocardial blood flow and hemodynamic variables in adenosine and regadenoson vasodilator 82-Rubidium PET. J Nucl Cardiol 29: 921–933
7. Mahmarian JJ, Peterson LE, Xu J, Cerqueira MD, Iskandrian AE, Bateman TM, Thomas GS, Nabi F (2015) Regadenoson provides perfusion results comparable to adenosine in heterogeneous patient populations: a quantitative analysis from the ADVANCE MPI trials. J Nucl Cardiol 22:248–261
8. Mahmarian JJ, Cerqueira MD, Iskandrian AE, Bateman TM, Thomas GS, Hendel RC, Moye LA, Olmsted AW (2009) Regadenoson induces comparable left ventricular perfusion defects as adenosine: a quantitative analysis from the ADVANCE MPI 2 trial. JACC Cardiovasc Imaging 2:959–968
9. Hendel RC, Bateman TM, Cerqueira MD, Iskandrian AE, Leppo JA, Blackburn B, Mahmarian JJ (2005) Initial clinical experience with regadenoson, a novel selective A2A agonist for pharmacologic stress single-photon emission computed tomography myocardial perfusion imaging. J Am Coll Cardiol 46:2069–2075
10. Kontraindikation Adenosin (n.d). https://www.gelbe-liste.de/wirkstoffe/Adenosin_10221. Accessed Oct 2025
11. Ananthasubramaniam K, Saval M, Van Harn M, Kitt TM, Kristy RM, Xu Y, Spalding JR (2022) Clinical experience with regadenoson SPECT myocardial perfusion imaging: insights into patient characteristics, safety, and impact of results on clinical management. Int J Cardiovasc Imaging 38:257–267
12. Asif T, Lee Chuy K, Malhotra S (2021) Asystole following regadenoson administration: review of literature, risk factors and management. J Nucl Cardiol Off Publ Am Soc Nucl Cardiol 28:2046–2055
13. Mustehsan MH, Gandhi H, Hasani A, Rashid SMI, Goldberg Y (2020) Regadenoson-induced asystole and ischemic EKG changes in the setting of underlying coronary disease. J Nucl Cardiol Off Publ Am Soc Nucl Cardiol 27:698–701
14. Derbas LA, Thomas GS, Medina CA, Abdel-Karim AA, Saeed IM, Bateman TM (2019) Severe bradycardia and asystole following regadenoson in pharmacological myocardial perfusion imaging: cases and treatment recommendations. JACC Cardiovasc Imaging 12:1288–1290
15. Rosenblatt J, Mooney D, Dunn T, Cohen M (2014) Asystole following regadenoson infusion in stable outpatients. J Nucl Cardiol 21:862–868
16. Underwood SR, Latus KA, Reyes E, Standbridge K, Walker S, Wechalekar K (2014) Regadenoson-induced bradycardia and hypotension: possible mechanism and antidote. J Nucl Cardiol 21:1040
17. Pandit A, Unzek Freiman S (2012) Complete heart block associated with regadenoson: a real side effect. J Nucl Cardiol 19:1236–1239
18. Andrikopoulou E, Morgan CJ, Brice L, Bajaj NS, Doppalapudi H, Iskandrian AE, Hage FG (2019) Incidence of atrioventricular block with vasodilator stress SPECT: a meta-analysis. J Nucl Cardiol 26:616–628
19. Agrawal V, Hosey C, Smith GT, Shah C (2018) Detrimental effects of nitroglycerin use during regadenoson vasodilator stress testing: a cautionary tale. J Nucl Cardiol 25:1718–1723
20. Doran JA, Sajjad W, Schneider MD, Gupta R, Mackin ML, Schwartz RG (2017) Aminophylline and caffeine for reversal of adverse symptoms associated with regadenoson SPECT MPI. J Nucl Cardiol 24:1062–1070
21. Jolly AF, Thomas GS (2017) Intravenous caffeine: an alternative to aminophylline to reverse adverse effects during regadenoson myocardial perfusion imaging. J Nucl Cardiol 24:1071–1074
22. Doukky R, Morales Demori R, Jain S, Kiriakos R, Mwansa V, Calvin JE (2012) Attenuation of the side effect profile of regadenoson: a randomized double-blinded placebo-controlled study with aminophylline in patients undergoing myocardial perfusion imaging. "The ASSUAGE trial." J Nucl Cardiol 19:448–457
23. Thomas GS, Tammelin BR, Schiffman GL, Marquez R, Rice DL, Milikien D, Mathur V (2008) Safety of regadenoson, a selective adenosine A2A agonist, in patients with chronic obstructive pulmonary disease: a randomized, double-blind, placebo-controlled trial (RegCOPD trial). J Nucl Cardiol 15:319–328
24. Prenner BM, Bukofzer S, Behm S, Feaheny K, McNutt BE (2012) A randomized, double-blind, placebo-controlled study assessing the safety and tolerability of regadenoson in subjects with asthma or chronic obstructive pulmonary disease. J Nucl Cardiol 19:681–692
25. Salgado-Garcia C, Jimenez-Heffernan A, Ramos-Font C, Lopez-Martin J, Sanchez-de-Mora E, Aroui T, Lopez-Aguilar R, Rivera-de-Los-Santos F, Ruiz-Frutos C (2016) Safety of regadenoson in patients with severe chronic obstructive pulmonary disease. Rev Esp Med Nucl Imagen Mol 35:283–286
26. Golzar Y, Doukky R (2014) Regadenoson use in patients with chronic obstructive pulmonary disease: the state of current knowledge. Int J Chron Obstruct Pulmon Dis 9:129–137
27. Leaker BR, O'Connor B, Hansel TT, Barnes PJ, Meng L, Mathur VS, Lieu HD (2008) Safety of regadenoson, an adenosine A2A receptor agonist for myocardial perfusion imaging, in mild asthma and moderate asthma patients: a randomized, double-blind, placebo-controlled trial. J Nucl Cardiol 15:329–336
28. Radwan SS, Schwartz OG (2019) Seizure: an adverse effect of regadenoson in myocardial perfusion imaging. Case Rep Cardiol 2019:6240605
29. Agarwal V, DePuey EG (2014) Regadenoson and seizures: a real clinical concern. J Nucl Cardiol Off Publ Am Soc Nucl Cardiol 21:869–870
30. Page RL 2nd, Spurck P, Bainbridge JL, Michalek J, Quaife RA (2012) Seizures associated with regadenoson: a case series. J Nucl Cardiol 19(2):389–391
31. Rapiscan (Regadenoson) (2014) Wichtige neue Hinweise zur Minimierung des Risikos einesSchlaganfalls und einer Verlängerung von Rapiscan-bedingten Anfällen nach der Anwendung von Aminophyllin. https://www.akdae.de/Arzneimittelsicherheit/RHB/Archiv/2014/20141222.pdf. Accessed Oct 2025
32. Elsadany M, McMahon SR, Mehla S, Duvall WL (2022) Hemiplegic migraine episode triggered by regadenoson. J Nucl Cardiol 29:3469–3473
33. Al Jaroudi W, Iskandrian AE (2009) Regadenoson: a new myocardial stress agent. J Am Coll Cardiol 54:1123–1130
34. Berlacher M, Mastouri R, Philips S, Skaar TC, Kreutz RP (2017) Common genetic polymorphisms of adenosine A2A receptor do not influence response to regadenoson. Pharmacogenomics 18:523–529
35. Elkholy KO, Hegazy O, Okunade A, Aktas S, Ajibawo T (2021) Regadenoson stress testing: a comprehensive review with a focused update. Cureus 13:e12940
36. Olah ME, Ren H, Stiles GL (1995) Adenosine receptors: protein and gene structure. Arch Int Pharmacodyn Ther 329:135–150
37. Olah ME, Stiles GL (1995) Adenosine receptor subtypes: characterization and therapeutic regulation. Annu Rev Pharmacol Toxicol 35:581–606
38. Lindner O, Bengel F, Burchert W, Dorr R, Hacker M, Schafer W, Schafers MA, Schmidt M, Schwaiger M, Vom Dahl J, Zimmermann R (2017) Myokard-perfusions-SPECT. Myocardial perfusion SPECT - Update S1 guideline. Nuklearmedizin 56:115–123

39. Pennell DJ, Mavrogeni SI, Forbat SM, Karwatowski SP, Underwood SR (1995) Adenosine combined with dynamic exercise for myocardial perfusion imaging. J Am Coll Cardiol 25:1300–1309
40. Reyes E, Pennell DJ (2010) Regadenoson for myocardial perfusion scintigraphy. Expert Opin Med Diagn 4:447–454
41. Palani G, Ananthasubramaniam K (2013) Regadenoson: review of its established role in myocardial perfusion imaging and emerging applications. Cardiol Rev 21:42–48
42. Gao Z, Li Z, Baker SP, Lasley RD, Meyer S, Elzein E, Palle V, Zablocki JA, Blackburn B, Belardinelli L (2001) Novel short-acting A2A adenosine receptor agonists for coronary vasodilation: inverse relationship between affinity and duration of action of A2A agonists. J Pharmacol Exp Ther 298:209–218
43. Pollack A, Nazif T, Mancini D, Weisz G (2013) Detection and imaging of cardiac allograft vasculopathy. JACC Cardiovasc Imaging 6:613–623
44. Burrage MK, Shanmuganathan M, Masi A, Hann E, Zhang Q, Popescu IA, Soundarajan R, Leal Pelado J, Chow K, Neubauer S, Piechnik SK, Ferreira VM (2021) Cardiovascular magnetic resonance stress and rest T1-mapping using regadenoson for detection of ischemic heart disease compared to healthy controls. Int J Cardiol 333:239–245
45. Bastarrika G, Ezponda A, Baizan AG, Calvo M, Pueyo JC, Gavira JJ, Caballeros M (2020) Safety of regadenoson for vasodilation in cardiac MRI stress tests. Radiologia (Engl Ed) 62:213–221
46. Pape M, Zacho HD, Aaroe J, Eggert Jensen S, Petersen LJ (2016) Safety and tolerability of regadenoson for myocardial perfusion imaging - first Danish experience. Scand Cardiovasc J 50:180–186
47. Beslic N, Milardovic R, Sadija A, Ceric S, Raic Z (2016) Regadenoson in myocardial perfusion study - first institutional experiences in Bosnia and Herzegovina. Acta Inform Med 24:405–408
48. Koutsikos J, Angelidis G, Zafeirakis A, Mamarelis I, Vogiatzis M, Ilia E, Lazaridis K, Demakopoulos N (2017) Performance and safety profile of regadenoson myocardial perfusion imaging: first experience in Greece. Hell J Nucl Med 20:232–236
49. Jager PL, Buiting M, Mouden M, Oostdijk AH, Timmer J, Knollema S (2014) Regadenoson as a new stress agent in myocardial perfusion imaging. Initial experience in The Netherlands. Revista Española de Medicina Nuclear e Imagen Molecular (English Edition) 33:346–351
50. Kattoor AJ, Kolkailah AA, Iskander F, Iskander M, Diep L, Khan R, Doukky R (2021) The prognostic value of regadenoson SPECT myocardial perfusion imaging: the largest cohort to date. J Nucl Cardiol Off Publ Am Soc Nucl Cardiol 28:2799–2807
51. Sidhu GS, Hendel RC (2021) The evolution of the prognostic value of regadenoson SPECT myocardial perfusion imaging. J Nucl Cardiol 28:2808–2811