Original Article
DOI:10.4274/mirt.galenos.2022.72593

Comparison of Regadenoson and Dipyridamole Safety Profile During Stress Myocardial Perfusion Imaging

Short title: Regadenoson and Dipyridamole Safety in MPI

Jan Roczniak,[1] Justyna Bączalska,[1] Gabriela Kanclerz,[1] Weronika Zielińska,[1] Joanna Ożga,[1] Błażej Cymerman,[1] Agnieszka Stępień MD, [2] Prof. Magdalena Kostkiewicz MD, PhD, [2,3] Katarzyna Holcman MD, PhD [2,3]

[1] Students' Scientific Group Medical Imaging in Cardiology, Jagiellonian University Medical College, Krakow, Poland
[2] Jagiellonian University Medical College, Department of Cardiac and Vascular Diseases, John Paul II Hospital, Krakow, Poland
[3] John Paul II Hospital, Department of Nuclear Medicine, Krakow, Poland

Corresponding Author Information
Jan Roczniak
roczniakjan@gmail.com
Telephone: 12 614 22 87
https://orcid.org/0000-0003-2536-2633
Received: 22.05.2022
Accepted: 15.08.2022
Online publication: 09.09.2022

Abstract
Background: The pharmacological stress test with vasodilator agents is an alternative cardiological diagnostic tool for patients with contraindications to the classical stress test provided by physical activity during the single photon emission computed tomography myocardial perfusion imaging.
Objective: The aim of our study was to compare the frequency of the side effects of regadenoson and dipyridamole during single photon emission computed tomography myocardial perfusion imaging.
Methods: This retrospective study included data of consecutive 283 patients who underwent pharmacological stress tests in years 2015-2020. The study group consisted of 240 patients who have received dipyridamole and 43 patients who have received regadenoson. The collected data included the patients' characteristics, the occurrence of side effects (divided into mild: headache, vertigo, nausea, vomiting, dyspnea, chest discomfort, hot flushes, general weakness and severe: bradycardia, hypotension, loss of consciousness) and blood pressure values/measurements.
Results: Overall, complications occurred relatively often (regadenoson: 23.2%, dipirydamol: 26.7%, p=0.639). Procedure discontinuation was necessary in 0.7% of examinations, whereas pharmacological support was necessary in 4.7%. There was no difference in prevalence of mild (regadenoson:16.2%, dipirydamol:18.3%, p=0.747) and severe complications (regadenoson:11.6%, dipyridamole: 15.0%, p=0.563). However, regadenoson has been found to cause a significantly smaller mean decrease of systolic blood pressure (regadenoson:-2.6±10.0mmHg, dipyridamole:-8.7±9.6mmHg, p=0.002), diastolic blood pressure (regadenoson: -0.9±5.4mmHg, dipyridamole:-3.6±6.2mmHg, p=0.032), as well as mean arterial pressure (regadenoson:-1.5±5.6 mmHg, dipyridamole:-5.4±6.5mmHg, p=0.001). **Conclusions**: Regadenoson and dipyridamole presented a similar safety profile during single photon emission computed tomography myocardial perfusion imaging. However, regadenoson has been found to cause significantly smaller decreases in systolic blood pressure, diastolic blood pressure, mean arterial pressure.

Introduction

Coronary artery disease (CAD) is a cardiovascular condition which involves atherosclerotic plaque formation in the vessel lumen. Due to impairment in the blood flow the oxygen delivery to the myocardium is disturbed(1). For this reason CAD is proved to be one of the main causes of death in developed and developing countries and should be properly diagnosed and treated (2).The single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is a non-invasive diagnostic tool which is performed in patients with suspected CAD. This method is a superior alternative to the treadmill electrocardiography test especially in patients with single-vessel CAD, with superior safety profile compared to the invasive diagnostic procedure, namely coronary arteriography (3,4). This imaging technique shows myocardial perfusion and the effects of

stress on the heart muscle. The SPECT myocardial perfusion imaging is a nuclear medicine imaging technique using gamma rays and radiopharmaceuticals such as Technetium-99m, it may be performed in one day or two day protocol (5). In one-day protocol the patient undergoes a rest SPECT scan in the morning and then a SPECT stress scan after 4 hours. In two-days protocol only one SPECT scan is taken daily. There are two strategies of stress testing. The most common is exercise on a treadmill with a constant heart rate, blood pressure and electrocardiographic (ECG) monitoring. The second technique is pharmacological and is used if the exercise test is contraindicated (6). During this method the patient receives one of the coronary vasodilators adenosine agonist: adenosine, regadenoson or dipyridamole. Dipyridamole is an indirect adenosine agonist, regadenoson and adenosine are direct agonists. Regadenoson is a selective α(2A) receptor agonist, while dipyridamole and adenosine can activate adenosine α(1), α(2A), α(2B) and α(3) receptors. These substances mimic physical exercise on the heart muscle (5). Each of the drugs applied to simulate cardiovascular stress causes various adverse effects due to the stimulation of adenosine receptors, most commonly: headache, chest pain, decrease in blood pressure, nausea (5). Therefore, it is important to compare the most commonly used vasodilators in terms of their safety profiles. The aim of the study was to compare regadenoson and dipyridamole in terms of complications and the impact on blood pressure during a SPECT examination.

Materials and Methods

Study included 283 consecutive patients who underwent pharmacological stress SPECT in years 2015-2020 in the John Paul II Hospital in Cracow, Poland. The study population consisted of two groups: 240 patients who had received dipyridamole (Persantin, Boehringer Ingelheim Pharmaceuticals Inc, Germany) and 43 patients who had received regadenoson (Rapiscan, GE Healthcare AS, Norway). The inclusion criteria were: having undergone a pharmacological stress SPECT with administration of dipyridamole or regadenoson, and age over 18 years old. Each patient included in the study gave informed consent to perform pharmacological stress SPECT. The exclusion criteria were the contraindications to the pharmacological stress with vasodilators (a history of severe bronchospasm, asthma during physical activity, severe aortic stenosis, severe obstructive hypertrophic cardiomyopathy, pregnancy or lactation, 2° or 3 ° degree, atrioventricular block and atrial node disease, arterial hypotension (SP < 90 mmHg) or history of allergic reaction to the previously mentioned drugs) (7). The collected data included the characteristics of the patients such as sex, age, BMI, medical information regarding chronic diseases like diabetes, hypertension, atherosclerosis, hyperlipidemia as well as past myocardial infarction or heart failure and the history of medical procedures (percutaneous coronary interventions, PCI, and coronary artery bypass graft surgery, CABG) as well as information regarding to the stress MPI procedure: side effects (divided into mild: headache, vertigo, nausea, vomiting, dyspnea, chest discomfort, hot flushes, overall weakness, and severe: bradycardia (defined as heart rate below 60), hypotension (defined as systolic blood pressure, SBP, <90 or mean blood pressure, MBP, <70) and loss of consciousness) and blood pressure measurements: before the procedure, 5 times during the procedure (every minute) and 4 times after the procedure (every minute). Standard descriptive statistics were used to describe the data. Categorical variables were presented as percentages. Quantitative data were presented as mean value ± 1SD (standard deviation) for data with normal distribution or median with interquartile range (Q1) -(Q3) (quartile 1 and 3, respectively) for data with distribution other than normal. Normality of the data was assessed using the Shapiro-Wilk test for samples smaller than 50 or Kolmogorov-Smirnov test for samples greater than 50. Quantitative variables with normal distribution were compared using the t-Student test. Non-normally distributed quantitative variables were compared using Mann-Whitney-Wilcoxon U test. Categorical variables were compared using Pearson's Chi-square test. The level of statistical significance was set at $p \leq 0.05$. All analyses were carried out with the software TIBCO Software Inc. (2017). Statistica (data analysis software system), version 13. http://statistica.io.

Study was provided with the ethical principles for clinical research based on the Declaration of Helsinki. Every patient included in the study gave informed consent for the SPECT examination. The Bioethics Committee of Jagiellonian University approved this study. It gave consent to the use of patients' health data related directly to the perfusion SPECT (the course of the procedure, complications, the measure given) as well as general information containing demographic data and information on general health for the purpose of conducting the study. The Bioethics Committee waived the obligation to obtain informed consent from enrolled patients due to the retrospective character of the study.

Results

The study group consisted of 283 patients who underwent pharmacological stress tests, 240 of whom have been administered dipyridamole and 43 regadenoson. The most common chronic condition was hypertension, followed by hyperlipidemia, atherosclerosis and obesity. Both groups were comparable in terms of chronic diseases, body mass index (BMI), past cardiovascular history: myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG); and others. Full characteristics of patients have been presented in the table below (Table 1).

Overall, complications occurred relatively often (regadenoson: in 10 of 43;23.2%, dipyridamole: in 64 of 240; 26.7%, p=0.639). The majority was mild complications (regadenoson: in 7 of 43; 16.2%, dipyridamole: in 44 of

240; 18.3%, p=0.747), however there was also a high occurrence of severe complications (regadenoson: in 5 of 43; 11.6%, dipyridamole: in 36 of 240; 15.0%, p=0.563). The difference between the two vasodilator drugs in terms of specific and pooled complications was not significant. Detailed comparison has been presented in Table 2.

The differences in mean blood pressure values (systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP)) during and before the procedure were presented in Table 3. Changes in SBP, DBP and MAP values in time compared between dipyridamole and regadenoson have been presented on Figure 1. Regadenoson has been found to cause a significantly smaller mean decrease of SBP (regadenoson:-2.6±10.0mmHg, dipyridamole:-8.7±9.6mmHg, p=0.002) and DBP (regadenoson: -0.9±5.4mmHg, dipyridamole:-3.6±6.2mmHg, p=0.032), as well as MAP (regadenoson:-1.5±5.6 mmHg, dipyridamole:-5.4±6.5mmHg, p=0.001) in comparison with the value before the procedure (Table 3) (Fig. 2A, 2B, 2C).

Discussion

In this study of the vasodilators' safety profile during MPI, the administration of dipyridamole was associated with a significant decrease in systolic (8.7±9.6 mmHg versus 2.6±10 mmHg, p=0.002), diastolic (3.6±6.2 mmHg versus 0.9±5.4 mmHg, p=0.032) and mean arterial pressure (5.4±6.5 mmHg versus 1.5±5.6 mmHg, p=0.001), in comparison to regadenoson. No such differences between the vasodilators were observed in terms of the symptoms reported by patients undergoing the procedure and the need of oxygen or aminophylline administration. The occurrence of any side-effects was observed in 10 of 43 patients (23.2%) in regadenoson, and 64 of 240 patients (26.7%) in the dipyridamole group (p=0.639). The main adverse effects of the vasodilator administration were: hypotension (reported by 38 of 283 patients, 13.4%, p=0.707), headache (15 of 283, 5.3%, p=0.092) and dyspnea (14 of 283, 4.9%, p=0.505). Presented data may suggest that regadenoson is safer to use than dipyridamole.

In the study conducted by Amer et al., regadenoson was associated with more frequent adverse effects (241 of 284, 84.9%) than dipyridamole (161 of 284, 56.7%) in patients undergoing MPI, with the p value <0.0001. There were particular types of complaints, which were statistically rarely observed in the dipyridamole group in comparison to regadenoson, which were: dyspnea (2.1% vs. 52.5%, p<0.0001), gastrointestinal discomfort (8.1% vs. 27.8%, p<0.0001) and chest pain (3.9 vs 15.8%, p <0.0001). Hypotension was very rare - 1.1% in the regadenoson and 0% in the dipyridamole group (8). In our study, there was no statistically significant difference of dyspnea in the dipyridamole group compared with regadenoson (4.6% vs. 7%, p=0.505). Hypotension was the most common complication both in the dipyridamole and regadenoson groups. Overall, complications were observed much more rarely in our study than in the study conducted by Amer et al."

Gaudarzi et al. investigated the hemodynamic responses to regadenoson and dipyridamole (9). The increase in the heart rate was significantly higher in the regadenoson group than in patients who received dipyridamole (34±14 vs. 23±10 beats per minute increase from baseline; p<0.01). Stress myocardial body flow and myocardial flow reserve were not different between the groups (2.2±0.6 vs. 2.1±0.6 ml/min/g, p=0.39, and 2.9±0.8 vs. 2.8±0.7, p=0.31, respectively). If we consider the most common side effects of regadenoson, in a study conducted by Katsikis et al., in the group of patients who underwent the MPI stress test, 197 of 279 women (71%) and 162 of 279 men (58%) experienced side effects of regadenoson. The following side effects occurred more frequently in women: chest pain (65 of 279, 23% versus 33 of 279, 12%, p=<0.001), gastrointestinal discomfort (55 of 279, 20% versus 33 of 279, 12%, p=0.01) dizziness (35 of 279, 12% versus 14 of 279, 5%, p=0.002) and headache (56 of 279, 20% versus 37 of 279, 13%, p=0.03) respectively in women and men. Other adverse appear to be unrelated to gender (10) In another study, the most common side effects of regadenoson were: dyspnea (149 of 232 patients, 64%), headache (45 of 232, 19%) and chest pain (39 of 232, 17%). Three patients (1.3%) required administration of pharmaceuticals or hemodynamic support to relieve their symptoms. If hemodynamic responses are considered, a significant (p<0.0001) drop in SBP and DBP was observed, as well as an increase in the heart rate (11).

Complications of regadenoson in our study were observed more rarely compared to those studies- dyspnea was present in 7% of patients, followed by overall weakness (4.6%) and no cases of headache and chest discomfort were reported. Hypotension occurred in 11.6% and bradycardia in 4.7% of patients administered with regadenoson. On the other hand, additional support was more often necessary - 4.7% of participants required administration of aminophylline, and 4.7% - oxygen."

Considering the relative potency of vasodilators, regadenoson produces higher stress myocardial blood flow (95 ± 11 vs. 86 ± 12 beats/minute) and myocardial perfusion reserve (3.11 ± 0.63 vs. 2.61 ± 0.57) than dipyridamole and if adjusted to the heart rate, has much higher heart rate response. It means that regadenoson has superior vasodilator efficacy to dipyridamole, therefore could be a better agent to perform the stress MPI test (12). In a survey-based study by Friedman et al. regadenoson and dipyridamole were compared in terms of duration of MPI test (156 vs. 191 min, respectively) and time from the administration to the start of the imaging procedure, including the dose calculation and infusion time, which were also shorter for regadenoson (mean difference: 12 min). Also, the time to manage the occurring adverse events was shorter in regadenoson (13).

It is worth adding that in the literature there is a certain trend in the popularity of using various vasodilators. In a survey study from 2013, the responders group consisted of the employees of healthcare facilities which perform MPI stress studies on the territory of the United States of America. In 93 of 141 (69%) imaging laboratories that took part in the survey only one agent had been used: in 38 (28%) adenosine, in 27 (20%) dipyridamole and in 28 (21%) regadenoson. From 141 labs, 36 (27%) used two agents, in 21 (16%) adenosine and regadenoson, in 8 (6%) adenosine and dipyridamole and in 7 (5%) dipyridamole and regadenoson. Only 6 (4%) labs used all three agents (13). In a similar study from 2020 35 of 50 (70%) participating labs were using only regadenoson, dipyridamole or adenosine were both used in only 3 (6%) of responders' place of work. There were 10 labs (20%) using two agents, one of which was regadenoson. In 7 (14%) the other one was dipyridamole and in 3 (6%) it was adenosine. Only 2 (4%) centers used all three agents (14).

Conclusions: Overall, based on our findings, regadenoson and dipyridamole presented a similar safety profile during single photon emission computed tomography myocardial perfusion imaging. There was no significant difference in the assessed complications. The occurrence of complications was high - overall: 26.1%, mild:18.0%, severe:14.4%. Procedure discontinuation was necessary in 0.7% of examinations, whereas pharmacological support was necessary in 4.7%. However, regadenoson has been found to cause significantly smaller decrease in systolic blood pressure, diastolic blood pressure, mean arterial pressure, so it might be preferred for patients with lower blood pressure or known tendency for hypotony.

Study limitations:

This is a retrospective, observational study with all of its inherent biases. There was a difference in the size of the groups in this study ,which could have impacted the results of statistical analysis. Duration of the symptoms was not taken into consideration, as it was not available in the documentation.

References

1. Shahjehan RD, Bhutta BS. Coronary Artery Disease. [Updated 2021 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564304/
2. Malakar AK, Choudhury D, Halder B, Paul P, Uddin A, Chakraborty S. A review on coronary artery disease, its risk factors, and therapeutics. J Cell Physiol. 2019 Aug;234(10):16812-16823. doi: 10.1002/jcp.28350. Epub 2019 Feb 20. PMID: 30790284.
3. Bokhari S, Shahzad A, Bergmann SR. Superiority of exercise myocardial perfusion imaging compared with the exercise ECG in the diagnosis of coronary artery disease. Coron Artery Dis. 2008 Sep;19(6):399-404. doi: 10.1097/MCA.0b013e3283021ab4. PMID: 18955833.
4. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020 Jan 14;41(3):407-477. doi: 10.1093/eurheartj/ehz425. Erratum in: Eur Heart J. 2020 Nov 21;41(44):4242. PMID: 31504439.
5. Henzlova MJ, Duvall WL, Einstein AJ, Travin MI, Verberne HJ. ASNC imaging guidelines for SPECT nuclear cardiology procedures: Stress, protocols, and tracers. J Nucl Cardiol. 2016 Jun;23(3):606-39. doi: 10.1007/s12350-015-0387-x. Erratum in: J Nucl Cardiol. 2016 Jun;23(3):640-2. PMID: 26914678.
6. Lak HM, Ranka S, Goyal A. Pharmacologic Stress Testing. 2021 Aug 2. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 32310423.
7. Rodrigues CVB, Oliveira A, Wiefels CC, Leão MS, Mesquita CT. Current Practices in Myocardial Perfusion Scintigraphy in Brazil and Adherence to the IAEA Recommendations: Results of a Cross-Sectional Study. Arq Bras Cardiol. 2018 Feb;110(2):175-180. doi: 10.5935/abc.20180023. PMID: 29561994; PMCID: PMC5855911.
8. Amer KA, Hurren JR, Edwin SB, Cohen G. Regadenoson versus Dipyridamole: A Comparison of the Frequency of Adverse Events in Patients Undergoing Myocardial Perfusion Imaging. Pharmacotherapy. 2017 Jun;37(6):657-661. doi: 10.1002/phar.1940. Epub 2017 May 26. PMID: 28475259.
9. Goudarzi B, Fukushima K, Bravo P, Merrill J, Bengel FM. Comparison of the myocardial blood flow response to regadenoson and dipyridamole: a quantitative analysis in patients referred for clinical 82Rb myocardial perfusion PET. Eur J Nucl Med Mol Imaging. 2011 Oct;38(10):1908-16. doi: 10.1007/s00259-011-1853-6. Epub 2011 Jun 9. PMID: 21656246.
10. Katsikis A, Kyrozi E, Manira V, Theodorakos A, Malamitsi J, Tsapaki V, Iakovou I, Voudris V, Kolovou G, Koutelou M. Gender-related differences in side-effects and hemodynamic response to regadenoson in patients undergoing SPECT myocardial perfusion imaging. Eur J Nucl Med Mol Imaging. 2019 Nov;46(12):2590-2600. doi: 10.1007/s00259-019-04463-9. Epub 2019 Aug 14. PMID: 31414207.
11. Pape M, Zacho HD, Aarøe J, Eggert Jensen S, Petersen LJ. Safety and tolerability of regadenoson for myocardial perfusion imaging - first Danish experience. Scand Cardiovasc J. 2016 Jun;50(3):180-6. doi: 10.3109/14017431.2016.1163415. Epub 2016 May 10. PMID: 26956081.

12. Vasu S, Bandettini WP, Hsu LY, Kellman P, Leung S, Mancini C, Shanbhag SM, Wilson J, Booker OJ, Arai AE. 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. 2013 Sep 24;15(1):85. doi: 10.1186/1532-429X-15-85. PMID: 24063278; PMCID: PMC3851492.
13. Friedman M, Spalding J, Kothari S, Wu Y, Gatt E, Boulanger L. Myocardial perfusion imaging laboratory efficiency with the use of regadenoson compared to adenosine and dipyridamole. J Med Econ. 2013;16(4):449-60. doi: 10.3111/13696998.2013.772057. Epub 2013 Feb 25. PMID: 23363331.
14. Yang H, Faust E, Gao E, Sethi S, Kitt TM, Kristy RM, Spalding JR, Xu Y. Evaluating the use of pharmacological stress agents during single-photon emission computed tomography myocardial perfusion imaging tests after inadequate exercise stress test. J Nucl Cardiol. 2021 Mar 11. doi: 10.1007/s12350-021-02546-5. Epub ahead of print. PMID: 33709333.

Tables

Table 1. Characteristics of the study group

	Total	**Regadenoson (n=43)**	**Dipirydamol (n=240)**	**p value**
Age (years)	70.4±9.2	71.0±7.4	70.3±9.5	0.638
Male sex	158 (55.8%)	24 (55.8%)	134 (55.8%)	0.993
BMI (kg/m2)	29.7±5.15	30.3±6.9	29.8±4.6	0.892
Obesity (BMI>30)	123 (43.5%)	17 (39.5%)	106 (44.2%)	0.639
Diabetes mellitus type 2	87 (30.9%)	10 (23.3%)	77 (32.2%)	0.241
Hypertension	227 (80.5%)	30 (69.8%)	197 (82.4%)	0.054
Atherosclerosis	139 (49.3%)	20 (46.5%)	119 (49.8%)	0.692
Hyperlipidemia	197 (69.5%)	31 (72.1%)	166 (69.5%)	0.729

Past MI	86 (30.5%)	11 (25.6%)	75 (31.4%)	0.447
Past PCI	89 (31.6%)	12 (27.9%)	77 (32.2%)	0.576
Past CABG	28 (9.93%)	4 (9.3%)	24 (10.0%)	0.881
Heart failure	118 (41.8%)	15 (34.9%)	103 (43.1%)	0.315

Quantitative data with normal distribution has been presented as mean±SD. Categorical variables have been presented as counts with percentages in brackets. BMI - body mass index; MI - myocardial infarction; PCI - percutaneous coronary intervention; CABG - coronary artery bypass grafting

Table 2. Detailed comparison of complications

	Total	**Regadenoson (n=43)**	**Dipyridamole (n=240)**	**p value**
Complications	74 (26.1%)	10 (23.2%)	64 (26.7%)	0.639
Mild complications:	51 (18.0%)	7 (16.2%)	44 (18.3%)	0.747
o Headache	15 (5.3%)	0	15 (6.25%)	0.092
o Vertigo	4 (1.4%)	1 (2.3%)	3 (1.3%)	0.582
o Nausea	1 (0.4%)	0	1 (0.4%)	0.672
o Vomiting	0	0	0	1.0
o Dyspnea	14 (4.9%)	3 (7.0%)	11 (4.6%)	0.505
o Chest discomfort	8 (2.8%)	0	8 (3.3%)	0.224
o Hot flushes	5 (1.8%)	0	5 (2.1%)	0.340

o Overall weakness	9 (3.1%)	2 (4.6%)	7 (2.9%)	0.551
Severe complications:	41 (14.4%)	5 (11.6%)	36 (15.0%)	0.563
o Bradycardia	6 (2.1%)	2 (4.7%)	4 (1.7%)	0.211
o Hypotension	38 (13.4%)	5 (11.6%)	33 (13.75%)	0.707
o Loss of consciousness	0	0	0	1
Procedure discontinuation	2 (0.7%)	0	2 (0.8%)	0.548
Aminophylline administration	14 (4.9%)	2 (4.7%)	12 (5.0%)	0.922
Oxygen administration	5 (1.8%)	2 (4.7%)	3 (1.3%)	0.119

Categorical variables have been presented as counts with percentages in brackets.

Table 3. Average change of blood pressure values during the procedure

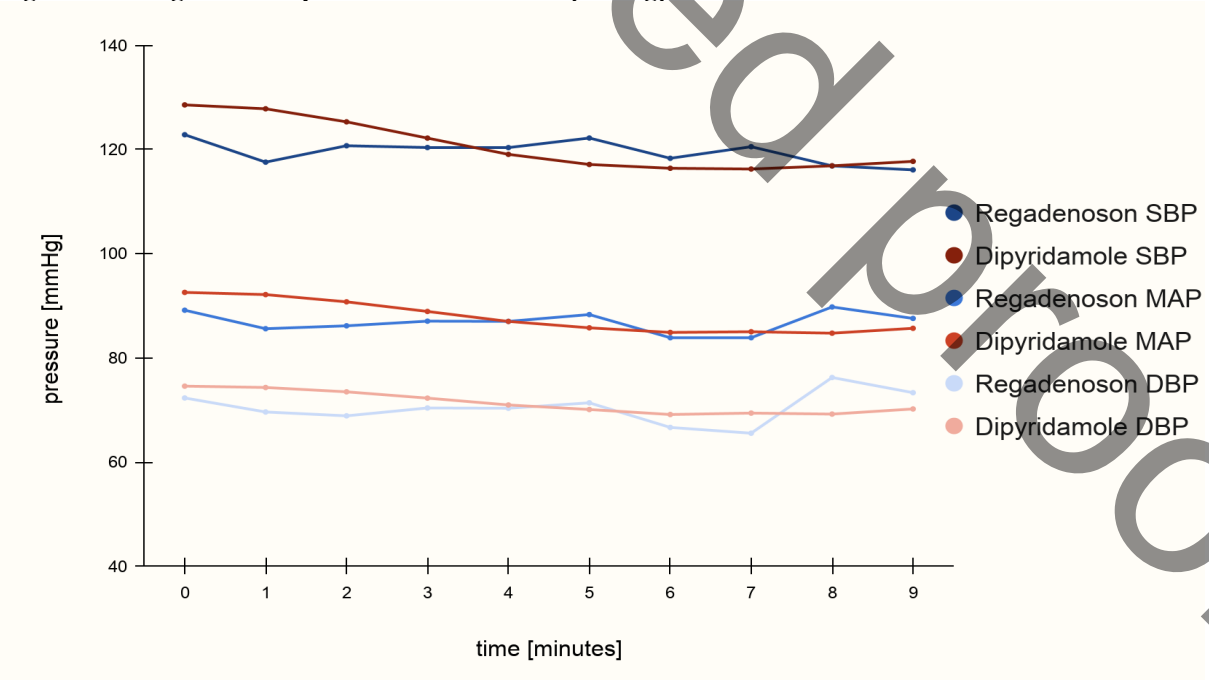
	Total	**Regadenoson (n=27)**	**Dipyridamole (n=240)**	**p value**

SBP change [mmHg]	**-8.1 ±9.8**	**-2.6 ±10.0**	**-8.7 ±9.6**	**0.002**
SBP change (% of initial value)	**-5.6 (-9.5)-(-1.0)**	**0 (-7.6)-(6.0)**	**-6.0 (-9.7)-(-1.7)**	**0.002**
DBP change [mmHg]	**-1.1 (-6.6)-(0.0)**	**0 (-4.0)-(0.0)**	**-1.1 (-7.8)-(0.0)**	**0.032**
DBP change (% of initial value)	-1.4 (-9.3)-(0.0)	0 (-5.0)-(0.0)	-1.6 (-9.7)-(0.0)	0.051
MAP change [mmHg]	**-4.0 (-8.1)-(-0.6)**	**-1.0 (-4.0)-(2.0)**	**-4.1 (-8.6)-(-1.2)**	**0.001**
MAP change (% of initial value)	**-4.1 (-8.73)-(-0.6)**	**-1.0 (-5.0)-(2.8)**	**-4.3 (-8.8)-(-1.2)**	**0.002**

Quantitative variables which followed normal distribution have been presented as mean±SD. Results with significant p values have been presented in **bold.** Positive value = increase, negative value = decrease.
SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure

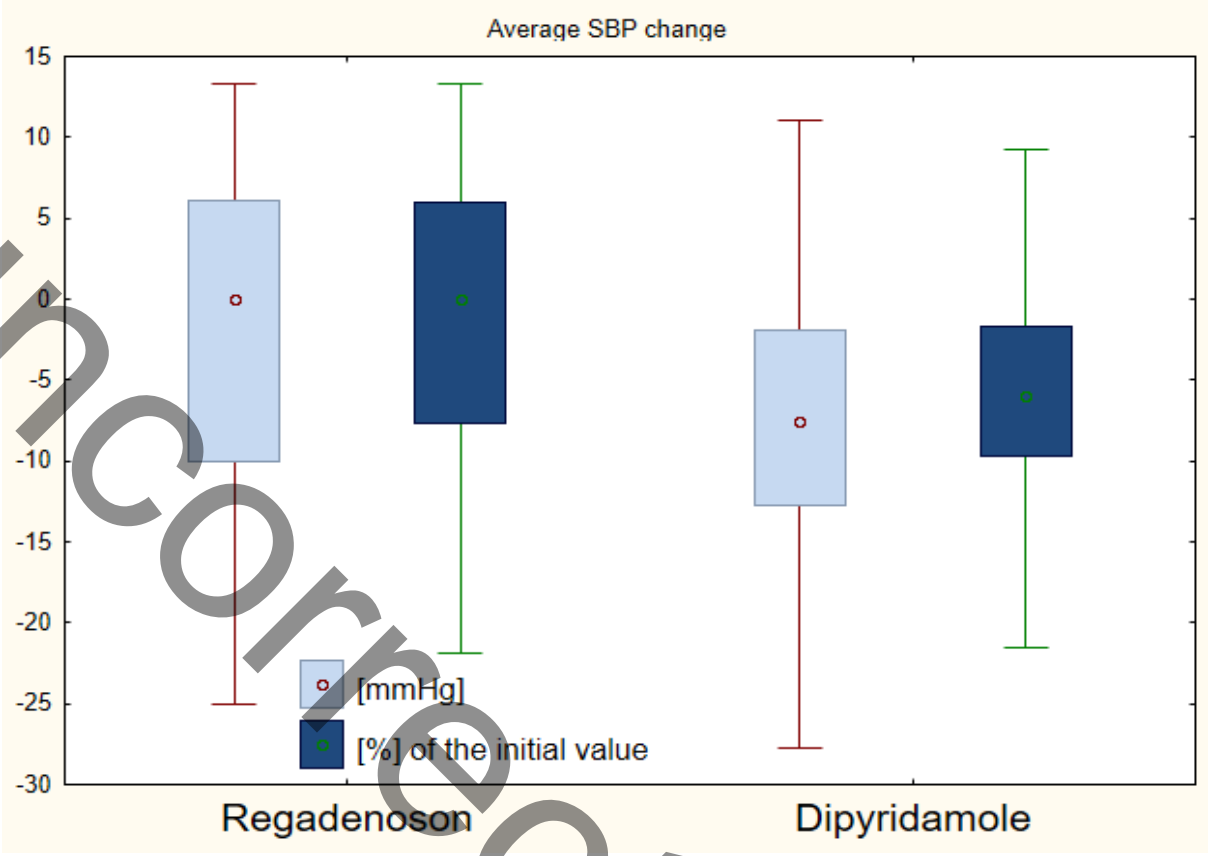
Figures

Figure 1. Change of blood pressure values in time [mmHg]



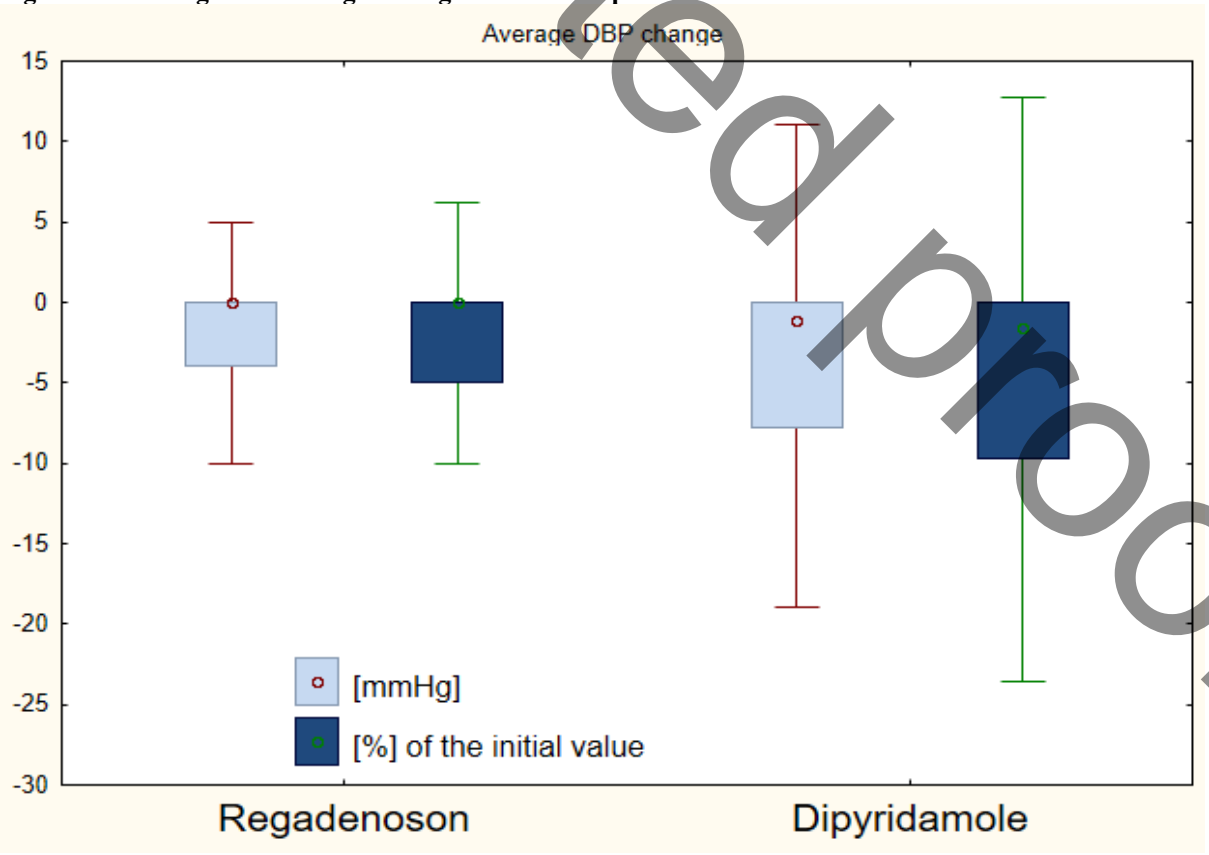
SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure

Figure 2A. Average SBP change during and after the procedure



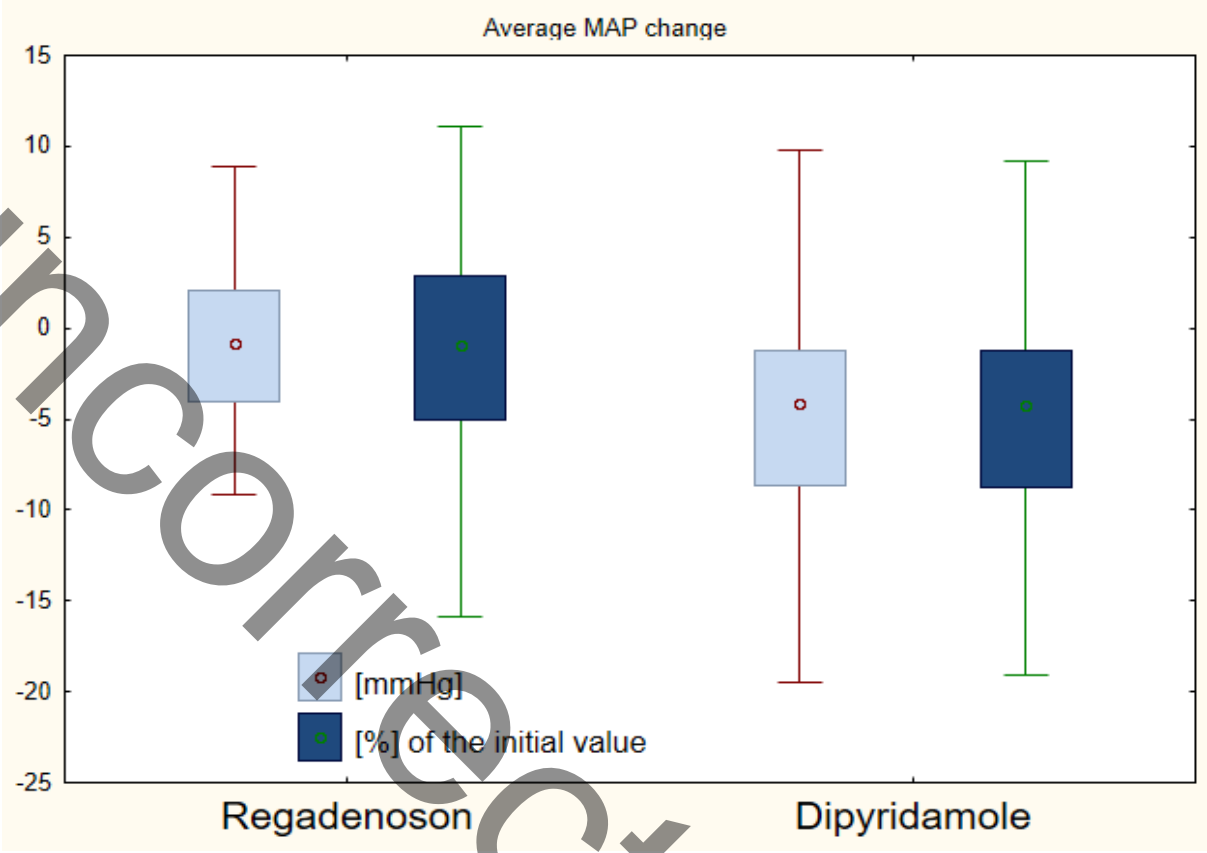
Data has been presented as median, quartiles and non-outlier range. SBP – systolic blood pressure

Figure 2B. Average DBP change during and after the procedure



Data has been presented as median, quartiles and non-outlier range. DBP – diastolic blood pressure

Figure 2C. Average MAP change during and after the procedure



Data has been presented as median, quartiles and non-outlier range. MAP – mean arterial pressure