Respiratory resistance of patients during cardiac stress testing with adenosine: Is dyspnea a sign of bronchospasm?

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Background. **Adenosine is widely used for stress-testing in myocardial perfusion imaging. During adenosine infusion, dyspnea is one of the main complaints of patients. The aim of this study was to determine whether dyspnea during adenosine infusion is caused by bronchospasm.**

Methods. **Fifty-four patients were enrolled in the study. Seven of these 54 suffered from mild chronic obstructive pulmonary disease (COPD). We continuously measured respiratory resistance (*R*rs), using impulse oscillometry. Respiratory resistance was measured before, during, and after a continuous infusion of 140 μg/kg/min adenosine.**

Results. **Sixty-seven percent of patients suffered from dyspnea during adenosine infusion. In patients with mild COPD, *R*rs was higher compared with other patients (0.48 vs 0.27 kPa/L/s, $P < .05$). Neither patients with COPD nor those without COPD exhibited a significant increase in *R*rs during adenosine infusion. The *R*rs of patients with dyspnea was insignificantly lower compared with patients without dyspnea ($P = .469$).**

Conclusions. **Dyspnea as a side effect of adenosine infusion is not correlated with impaired respiratory resistance in nonasthmatic patients and in patients with mild COPD. Thus bronchospasm is ruled out as cause of this clinical symptom. Despite the small number of COPD patients enrolled in the study, adenosine infusion might be possible in patients with mild COPD. (J Nucl Cardiol 2008;15:94-9.)**

Key Words: Adenosine • dyspnea • respiratory resistance • forced oscillation technique

The endogenous nucleoside adenosine is widely used for stress-testing in myocardial perfusion imaging. In 2005, vasodilatation with adenosine or dipyridamole was applied in 21% of all myocardial scintigraphies in Germany.[1] The frequency of pharmacologic stress-testing might even rise in the future due to the higher number of patients who are unable to perform an exercise stress test because of age, multiple morbidities, or implanted pacemakers. The diagnostic performance of myocardial scintigraphy with adenosine stress-testing is good compared with that of exercise tests.[2]

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During adenosine infusion, dyspnea is one of the main complaints of patients.[3,4] In spite of the large number of patients suffering from dyspnea, severe events of bronchospasm during adenosine stress are rare. In a multicenter trial on the safety of adenosine, including 9256 patients, seven episodes of severe bronchospasm were observed.[5]

The forced-oscillation technique was shown to be reliable for measuring respiratory resistance, with minimal requirements for the subject's cooperation.[6] It averts the need for any special breathing maneuver, and allows continuous measurement of respiratory resistance during pharmacologic interventions. The aim of this study was to determine whether dyspnea during adenosine cardiac stress testing is related to changes in respiratory resistance.

METHODS

Patient Population

Sixty-eight consecutive patients entered the study and gave informed consent during study enrollment. All patients were referred to our department for myocardial perfusion

Table 1. Respiratory resistance of all 54 patients (kPa/l/s) at 21 measurement points extracted from continuous measurement

Time (seconds)	Mean ± SD	Adenosine infusion
0	0.31 ± 0.25	No
30	0.30 ± 0.26	No
60	0.30 ± 0.28	No
90	**0.31 ± 0.28**	**Yes**
120	**0.30 ± 0.29**	**Yes**
150	**0.29 ± 0.26**	**Yes**
180	**0.29 ± 0.28**	**Yes**
210	**0.29 ± 0.28**	**Yes**
240	**0.29 ± 0.28**	**Yes**
270	**0.28 ± 0.25**	**Yes**
300	**0.29 ± 0.27**	**Yes**
330	**0.29 ± 0.25**	**Yes**
360	**0.30 ± 0.26**	**Yes**
390	**0.30 ± 0.28**	**Yes**
420	**0.30 ± 0.28**	**Yes**
450	0.28 ± 0.23	No
480	0.27 ± 0.22	No
510	0.28 ± 0.23	No
540	0.28 ± 0.24	No
570	0.27 ± 0.23	No
600	0.28 ± 0.23	No

Boldface indicates results during adenosine infusion.

scintigraphy, either to rule out the existence of coronary artery disease (CAD), or to test for the functional relevance of existing CAD. The adenosine stress-test was chosen because of the inability of patients to perform exercise testing. In 14 of 68 patients, the measurement of respiratory resistance had to be aborted, and these patients were excluded from further analysis. The reasons for the abort involved nausea in five patients, heavy coughing in another five patients, indisposition because of symptomatic atrioventricular blocking in three patients, and hypotension in one patient.

The majority of the remaining 54 patients were male (42/54). The mean age was 64.2 years for male patients, and 69.0 years for female patients. The mean body mass index of patients was 28.7 kg/m^2. Seven patients suffered from chronic obstructive pulmonary disease (COPD). According to the recommendations of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), the results of spirometry were defined as stage I in five patients, and stage II in the remaining two patients.[7] Nine patients were current smokers, and 24 were former smokers.

Stress Protocol

All investigations took place between 9 and 11 AM. Patients were placed in sitting position. An electrocardiogram

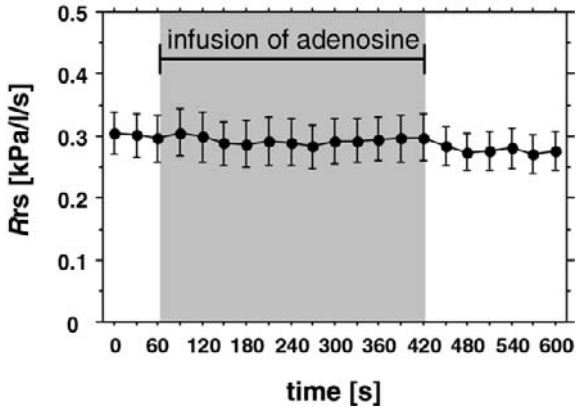

Figure 1. Mean values ± standard errors of respiratory resistance (*R*rs) of all 54 patients before, during, and after adenosine infusion. No significant increase or decrease in *R*rs occurred during adenosine infusion. *s,* seconds.

was recorded continuously, and blood pressure was measured every minute. Pharmacologic stress with adenosine (0.14 mg/kg body weight/min, Adenoscan, Sanofi-Aventis, Frankfurt, Germany) was performed for 6 minutes. The tracer was injected after 3 minutes of infusion.

Measurement of Respiratory Resistance

Respiratory resistance was measured by the use of impulse oscillometry at 10 Hz (System Power Cube, Ganshorn, Germany). The principle of the forced-oscillation technique (FOT) was described in further detail elsewhere.[6] In brief, FOT employs small-amplitude pressure oscillations superimposed upon normal breathing. Respiratory resistance is measured by comparing the propagation of the oscillating air flow in the respiratory system with that in a reference tube with known resistance. Resistance is calculated using Ohm's law by dividing the pressure difference (Pa = pascal) by airflow (liters per second). Here, respiratory resistance is given in kilopascals per liter per second (kPa/L/s).

After warming up the device for 30 minutes, a daily calibration was performed. Before starting a measurement, the nose of the patient was closed with a nose clip, and the patient was trained to breath through the mouthpiece with tightened lips. After an individual training period, measurement began. Respiratory resistance was recorded for 10 minutes, starting 1 minute before adenosine infusion. No special breathing maneuvers had to be performed.

Resistance curves for the whole measurement period were transferred to a personal computer. For each patient, 21 values were selected manually, one value for every 30 seconds. This procedure ensured that no artificial values entered the analysis, eg, because of swallowing by the patients. Three values were taken before adenosine infusion, 12 during adenosine infusion, and six after adenosine infusion.