

## COMPARISON OF DOBUTAMINE ELECTROCARDIOGRAPHIC STRESS TEST AND EXERCISE TEST IN TWO DIFFERENT GROUPS OF PATIENTS WITH UNSTABLE ANGINA

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**Summary** Exercise testing is a well known means of evaluating patients with unstable angina, but in recent years, alternative methods have been proposed. We prospectively compared standard exercise testing with dobutamine electrocardiographic stress testing for patients who were admitted with a diagnosis of unstable angina. A total of 43 patients were studied, divided into two different groups, according to the presence (group A  $n = 26$ ) or absence (group B  $n = 17$ ) of a previous history of coronary artery disease and/or electrocardiographic changes compatible with ischemia on admission. Dobutamine electrocardiographic stress testing was performed in a standard manner at  $3 \pm 1$  days after admission in group A and at  $16 \pm 8$  hours after admission in group B. Exercise testing was performed, on average  $5 \pm 1$  days following the event in group A and 2 days after admission in group B. Agreement between both tests was observed in 39 (91%) cases, Kappa value: 0.81. The dobutamine test predicted the result of the exercise test with a sensitivity of 79% (95% CI 54-90), and a specificity of 100% (95% CI 86-100), with a positive predictive value of 100% and a negative predictive value of 86%. It can be concluded that dobutamine electrocardiographic stress testing is an objective and reliable procedure that accurately predicts the results of standard exercise testing in patients with a diagnosis of unstable angina. If this result were confirmed with a greater number of patients, it would be a good option for definitive diagnosis and risk stratification, in addition to being inexpensive and easy to perform. It can also be particularly useful for patients who cannot perform exercise.

**Key words:** unstable angina, risk stratification, dobutamine electrocardiographic stress test, exercise stress test

Risk stratification after unstable angina is the subject of numerous studies, due to the need to select appropriate invasive procedures for the most serious cases. Despite the predictive value of the clinical form and the response to treatment, most patients rapidly stabilize, raising the question of how best to proceed. Traditional exercise testing after unstable angina has proved to be a

safe, effective and widely available method of risk stratification. However, many patients are unable to perform exercise owing to advanced age, lung diseases, peripheral vascular disorders or osteomuscular affections of the lower limbs. As a result, alternative method of pharmacological stress controlled with echocardiography or scintigraphy have been developed. The results of dobutamine electrocardiographic stress testing in cases of an acute myocardial infarct are promising but data are scarce concerning its use in cases of unstable angina.

Our first objective was prospectively to compare the results of standard exercise testing with

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those of dobutamine electrocardiographic stress testing in risk stratification after unstable angina, previously stabilized with pharmacological treatment. A second objective was to try to make precise diagnosis and prognosis of patients with suspected unstable angina who have no previous history of coronary illness, or old or new ischemic electrocardiographic abnormalities.

## Material and methods

### Patients

A total of 43 consecutive patients admitted for unstable angina (17 men and 26 women) with an average age of 61 ( $\pm 10$  years) were included in the study. The clinical characteristics and treatment of the study population are shown in Table I.

The diagnosis of unstable angina was based on a clinical history of chest pain occurring with or without ECG ischemic changes, either with increasing frequency at rest or with minimal exercise; for a period of 20 minutes or longer; or within 1 month of the onset of angina of New York Heart Association functional class III or IV. Serum levels of creatine kinase less than twice the normal upper limit were also considered. All patients were admitted within 24 hours of the onset of symptoms and their condition stabilized with medical treatment.

The population was divided into two groups: Group A comprised unstable angina patients whose condition stabilized with medical treatment. Exercise testing and electrocardiographic stress testing were compared for risk stratification. Group B was formed of patients admit-

ted to the Coronary Unit with suspected unstable angina who had no previous history of coronary illness and who did not show electrocardiographic disorders suggesting previous infarction or acute ischemia. Both tests were used on this group in order to confirm the diagnosis of unstable angina. The comparative study of the two test was carried out without suspending medication. Group A was given conventional treatment for unstable angina including the necessary dose of beta-blockers. For Group B only nitrates and aspirin were administered. Given the differences between the two groups and between the aims of their respective studies, the two tests were carried out with a greater precision in Group B than in Group A.

Patients were excluded if the application or interpretation of the exercise test was precluded for any reason; namely, patients over 80 years old and those suffering severe heart failure, serious rhythm abnormalities, left bundle branch block, WPW syndrome, or any other electrocardiographic abnormality known to affect ST segment analysis. Patients with valvular, congenital or myocardial diseases were also excluded.

### Dobutamine electrocardiographic stress test

Dobutamine electrocardiographic stress testing was performed 3  $\pm$  1 days after a patient's clinical stabilization in group A and after 16  $\pm$  8 hours in group B. An intravenous infusion of dobutamine began with a dose of 5 mcg/kg/min, then progressively increased every 5 minutes up to 40 mcg/kg/min. Cuff blood pressure was measured and a 12 lead ECG was recorded at baseline, after each dose, and 5 and 10 minutes after completing the infusion.

Test results were considered positive when there was evidence either of typical anginal pain or horizontal or down-sloping ST segment changes of at least 1 mm, 80 milliseconds after the J point, in three consecutive beats in at least two leads. Tests that were completed without this ischemic response were considered negative.

### Standard exercise test

Exercise testing was performed on a treadmill using the Naughton protocol 5  $\pm$  1 days after the patient's clinical stabilization in group A and after 2 days in group B.

A 12 lead ECG was recorded at baseline. Leads DII, V2 and V5 were continuously monitored during the test. Recordings were taken at the end of each stage and at minutes 1, 3 and 5 of recovery, or until the patients' condition normalized. Blood pressure was measured during the last minute of each stage and at minutes 1, 3 and 5 of recovery.

Test results were considered positive when either typical anginal pain began or horizontal or downsloping ST segment changes of a least 1mm, 80 milliseconds after the J point, were present. Tests that were completed without this ischemic response were considered negative.

The exercise test was always performed after the dobutamine electrocardiographic stress test, and the staff

TABLE 1. *Clinical characteristics of the study group*

<b>Group A (n = 26):</b>	
Age, years mean $\pm$ SD	65 $\pm$ 8
Male / Female, n	15 / 11
Treatment, n (%)	
beta-blockers	25 (96)
aspirin	25 (96)
oral nitrates	26 (100)
calcium antagonists	1 (4)
anticoagulation	8 (31)
<b>Group B (n = 17)</b>	
Age, years mean $\pm$ SD	55 $\pm$ 11
Male / Female, n	7 / 10
Treatment, n (%)	
aspirin	17
intravenous nitroglycerin	17



cardiologist who performed it was unaware of the results of the previous test.

#### Statistical analysis

Results are reported as the mean value  $\pm$  SD. Student's t-tests were used to compare the means of continuous variables. To evaluate the statistical significance of the relationship between variables obtained from the two tests, Fisher's exact test was used. A p value of  $< 0.05$  was considered significant. Sensitivity, specificity, positive predictive value and negative predictive value of the dobutamine test as compared with the standard exercise test, and the 95% confidence intervals were calculated according to standard definitions. Agreement between dobutamine and exercise tests was defined by the percentage of concordant diagnoses and also by a calculation of the Kappa value.

## Results

#### Dobutamine electrocardiographic stress test

The dobutamine tests were positive in 15 patients (35%) and negative in the remainder. Among the positive cases, 10 (67%) had ST segment depression and 5 (33%) had angina alone. Of the patients with ST segment depression, it was isolated in 7 (47%) and associated with angina in 3 (20%) (Fig. 1).

The test was positive in 8 patients of group A (31%) and in 7 patients of group B (41%), p NS.

Between rest and the maximal dobutamine dose heart rate increased from  $63 \pm 9$  bpm to  $102 \pm 23$  bpm ( $p < 0.001$ ). Systolic blood pressure and the double product increased from  $117 \pm 20$  mmHg to  $141 \pm 29$  mmHg and from  $7502 \pm 1916$  to  $14251 \pm 473$ , respectively ( $p < 0.01$ ). The threshold double product was  $13000 \pm 4400$ .

Both base double product and maximal double product were greater in group B than in group A ( $8369 \pm 1439$  vs  $6823 \pm 1764$ ,  $p < 0.05$ , and  $16172 \pm 5163$  vs  $12615 \pm 3918$ ,  $p < 0.05$  respectively).

Mild symptoms such as palpitations, headache or chills were present in some patients but in no case were they considered clinically important and always disappeared a few minutes after the infusion had been concluded.

#### Standard exercise test

The exercise test was positive in 19 patients (44%) and negative in the remainder. Nine patients (47%) had ST segment depression alone,

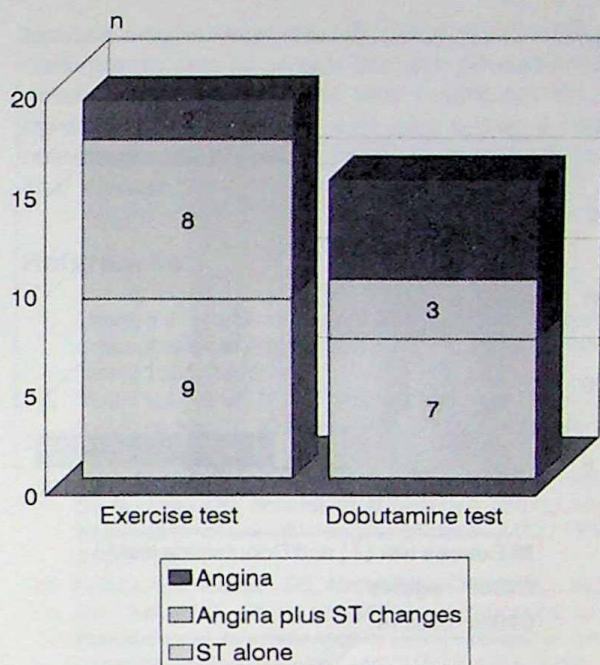


Figure 1

8 (42%) had ST segment depression and angina, and 2 (11%) had angina alone (Fig. 1). The test was positive in 7 (27%) cases in the group A, and in 12 (70%) patients in the group B.

Heart rate increased from  $63 \pm 9$  bpm to  $99 \pm 23$  bpm ( $p < 0.05$ ), the double product increased from  $7153 \pm 2315$  to  $14591 \pm 5401$  ( $p = 0.05$ ), and the systolic blood pressure from  $117 \pm 20$  mm Hg to  $141 \pm 29$  mm Hg ( $p < 0.05$ ). The threshold double product was  $13700 \pm 4200$ .

The average workload achieved was  $6.2 \pm 2.6$  METS. The average workload that provoked ischemic response was  $4.8 \pm 2.1$  METS.

Both base double product and maximal double product were greater in group B than in group A ( $7505 \pm 1479$  vs.  $6900 \pm 1074$ ,  $p < 0.05$ , and  $21000 \pm 4625$  vs.  $13430 \pm 4215$ ,  $p < 0.05$  respectively). As in the case of the dobutamine electrocardiographic stress test this difference was attributed to the use of beta-blocker treatment in Group A.

#### Comparison of the two tests

Neither test produced significant differences in maximal double product, heart rate or systolic blood pressure.

In both tests 24 patients (56%) were negative and 15 (35%) positive, with an overall agreement



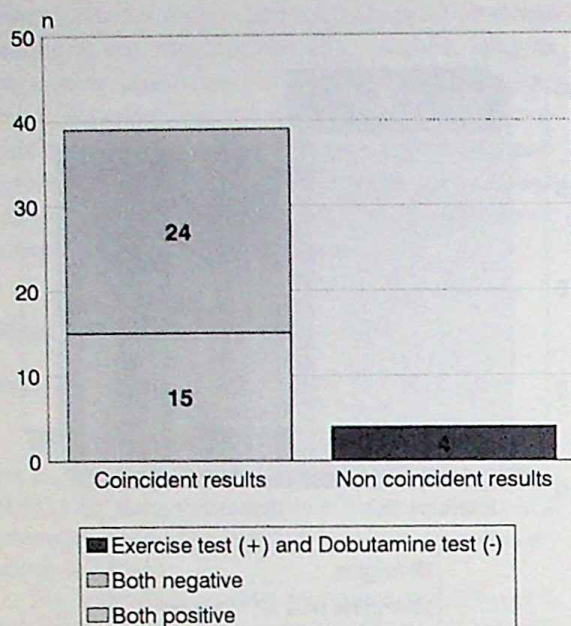


Figure 2

of 91% between the two methods ( $p < 0.001$ , Kappa: 0.81). Only 4 patients (9%) were discordant, all of whom demonstrated positive responses in their exercise tests and negative responses in their dobutamine tests.

The overall agreement was 96% (Kappa = 0.92) in Group A and 83% (Kappa = 0.67) in Group B.

The dobutamine stress test predicted the results of the standard exercise test with a sensitivity of 79% (95% CI = 54 - 90) and a specificity of 100% (95% CI = 86 - 100), with a positive predictive value of 100% and a negative predictive value of 84%.

## Discussion

It has been demonstrated that exercise testing has a prognostic value for patients with a diagnosis of unstable angina who became asymptomatic with medical treatment.<sup>1-6</sup> Nevertheless, it is necessary to evaluate alternative methods since a variable proportion of patients are unable to perform exercises due to physical or cardiac contraindications<sup>4-7</sup>. The use of these alternative methods, including pharmacological stress using dobutamine, adenosine or dipyridamole controlled with echocardiography or scintigraphy is expand-

ing rapidly, making their evaluation particularly important.

At the same time it could be useful to reduce the time spent in the Coronary Unit by patients who are less at risk of suffering complications or, despite a characteristic clinical profile, have a more favorable prognosis.

In this study we have made a prospective comparison of the routine practice of exercise testing with dobutamine electrocardiographic stress testing. The latter is probably less sensitive and less specific than more sophisticated tests, but it has the advantage of being objective, safe inexpensive, and potentially very useful for patients who are unable to perform exercises. In addition, dobutamine electrocardiographic stress test is easy to perform and interpret, does not require special medical training and could be widely available. In comparing the results of the two procedures, concordance was found in positive and negative results, in the type of positivity, and also in the localization of electrocardiographic ischemic changes.

The concordance between the two tests was somewhat higher than that found in previous studies<sup>8-11</sup>, from which the present study differed in that it was prospective, the tests were performed earlier, the dobutamine doses were higher, all 12 ECG leads were recorded, the patients were medically treated as necessary and we did not take into account ST segment elevation, owing to the difficulties involved in its interpretation.

Furthermore, most studies of electrocardiographic stress testing have focused on patients with acute myocardial infarction, whereas reports concerning unstable angina are scarce.<sup>14</sup>

The values of the concordance between electrocardiographic stress testing and exercise testing were similar in both groups, but in group A the objective was risk stratification, while in group B the purpose of the test was diagnosis. The number of patients analyzed in either group, did not allow definitive conclusions concerning sensibility, specificity or positive and negative predicted values separately.

Although further studies with a greater number of patients are necessary, dobutamine stress testing does appear to have an important role in predicting the results of standard exercise testing for risk stratification after unstable angina as well as for the confirmation of the diagnosis.



## Resumen

*Comparación del test de dobutamina con el control electrocardiográfico en pacientes con angina inestable*

La ergometría es un procedimiento bien conocido para evaluar a los pacientes que presentan angina inestable. Sin embargo, en los últimos años han sido propuestos otros métodos alternativos. La mayoría de ellos son sofisticados, necesitan de tecnología compleja y operadores particularmente entrenados. En este estudio hemos comparado prospectivamente un procedimiento muy difundido como la ergometría, con otro sencillo y de fácil realización como el test de dobutamina con control electrocardiográfico, en pacientes que fueron internados en la Unidad Coronaria con diagnóstico de angina inestable.

Se analizaron 43 pacientes consecutivos, quienes a su vez fueron divididos en dos subgrupos, de acuerdo a la presencia (Grupo A,  $n = 26$ ) o ausencia (Grupo B,  $n = 17$ ) de historia previa de enfermedad coronaria y/o cambios electrocardiográficos compatibles con isquemia al ingreso. El test de dobutamina controlado con electrocardiografía fue realizado en el Grupo A a los  $3 \pm 1$  días después del ingreso en los pacientes que se lograron estabilizar con tratamiento médico y en el Grupo B a las  $16 \pm 8$  hs de la admisión. La ergometría fue realizada en el Grupo A a los  $5 \pm 1$  días luego del evento y en el Grupo B 2 días luego de la internación. En el grupo A la comparación se realizó con el objeto de analizar la posible eficacia del test de dobutamina con control electrocardiográfico en la estratificación de riesgo coronario de los pacientes controlados con el tratamiento. En el grupo B el propósito fue conocer su utilidad en el diagnóstico de angina inestable.

Se observó concordancia entre los dos métodos analizados en 39 (91%) de los pacientes, Kappa 0,81. Al analizarse por separado ambos grupos el valor de la concordancia se objetivó en un índice Kappa que en el grupo A resultó de 0,92 (96%) y en el grupo B de 0,67 (83%).

En la totalidad de los pacientes el test de dobutamina predijo el resultado de la ergometría con una sensibilidad del 79% (95% IC 54-90) y una especificidad del 100% (95% IC 86-100). El valor predictivo negativo fue del 86% y el predictivo positivo del 100%.

El test de dobutamina controlado con electrocardiografía resultó ser un procedimiento objetivo, con alta confiabilidad para predecir los resultados de la ergometría convencional en pacien-

tes con angina inestable. Si estos resultados se confirmaran con un mayor número de pacientes, podría convertirse en una muy buena opción, al resultar fácil de realizar, con bajo costo, y particularmente útil en pacientes que no pueden realizar ejercicio.

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