

## Stress echocardiography in the pre-operative evaluation of patients undergoing major vascular surgery: are results comparable with dipyridamole versus dobutamine stress echo?

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**Introduction.** Perioperative cardiovascular complications are an important cause of post-surgical morbidity and mortality in patients undergoing major vascular surgery. Dobutamine Stress Echo is considered one of the methods of choice in the detection of coronary artery disease in this subgroup of patients.

**Objectives.** Our aim was to analyze if dipyridamole stress echocardiography could be used as an alternative to Dobutamine Stress Echo in the perioperative evaluation of patients in need of major vascular surgery.

**Patients and method.** The result of consecutive dipyridamole and dobutamine stress exams prior to vascular surgery were reviewed. We analyzed if those patients with a positive stress echo presented a higher number of cardiac events during and after surgery than those with negative stress echo. The negative and positive predictive values were calculated for both techniques.

**Results.** 133 stress exams were analysed: 39 with dobutamine and 94 with dipyridamole. Of the 39 dobutamine studies 2 were positive, 29 negatives and 8 non conclusive. Of the 94 dipyridamole studies 13 were positive and 81 negatives. None of the patients with a positive dobutamine echo underwent surgery. The negative predictive value for dobutamine echo was 96.5%, quite similar to that of dipyridamole stress echo (97.5%).

**Conclusion.** Dipyridamole stress echocardiography is a valid alternative to dobutamine echocardiography in the pre-surgical evaluation of patients undergoing major vascular surgery.

**Key words:** *Stress. Surgery.*

### **Ecocardiografía de estrés en el preoperatorio de cirugía vascular: ¿son comparables los resultados con dipiridamol y dobutamina?**

**Introducción.** Las complicaciones cardiovasculares perioperatorias son causa de morbimortalidad posquirúrgica en pacientes sometidos a cirugía vascular. La ecocardiografía de estrés se usa como cribado para la detección de enfermedad coronaria en estos pacientes.

**Objetivos.** El propósito del estudio es analizar si la ecocardiografía de estrés con dipiridamol puede ser usada como alternativa a la ecocardiografía con dobutamina en la estratificación pronóstica de los pacientes que requieren cirugía vascular mayor.

**Pacientes y método.** Se revisaron las ecocardiografías de estrés con dobutamina y dipiridamol realizadas antes de la cirugía vascular. Se analizó si los pacientes con resultado positivo presentaron un mayor número de acontecimientos cardíacos durante y tras la cirugía que aquellos con prueba negativa. Se calcularon los valores predictivos positivos y negativos de ambas técnicas.

**Resultados.** Se han analizado 133 ecocardiogramas de estrés. De éstos, 39 se realizaron con dobutamina y 94 con dipiridamol. De los 39 estudios con dobutamina, dos fueron positivos, 29 negativos y ocho no concluyentes. De los 94 estudios con dipiridamol, 13 eran positivos y 81 negativos. Ninguno de los pacientes con ecocardiograma con dobutamina positivo fue intervenido. El valor predictivo negativo para la dobutamina fue de 96,5%, muy similar al del dipiridamol (97,5%).

**Conclusiones.** La ecocardiografía de estrés con dipiridamol es una alternativa válida a la ecocardiografía con dobutamina en la valoración prequirúrgica de los pacientes que van a ser sometidos a cirugía vascular mayor.

**Palabras clave:** *Estrés. Cirugía.*

### **INTRODUCTION**

The prevalence of severe coronary artery disease in patients who undergo major vascular surgery is high, about 28%-36%. Many of these patients are asymptomatic and their identification is sometimes complex.

Perioperative cardiovascular complications, like acute myocardial infarction, acute lung edema, and malig-

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## ABBREVIATIONS

SE: stress echocardiography

nant ventricular arrhythmias are an important cause of mortality and postsurgical morbidity in this such patients.

Screening for coronary artery disease in patients who undergo major vascular surgery allows the detection of high-risk patients and prevention of cardiac events during and after surgery by previous coronary revascularization, the realization of a less aggressive surgical intervention than initially programmed, administration of additional perioperative medication, and/or intensive intra and postoperative monitoring.

Since many of these patients are incapable of performing a stress test because their capacity for physical effort is limited, technical alternatives have been sought, like ambulatory monitoring of the ECG, radio-nuclide perfusion study, and dobutamine stress echocardiography.

Stress echocardiography (SE) with dobutamine is currently considered the technique of choice in the preoperative assessment of these patients. Given the existence of patients in whom dobutamine administration is contraindicated (severe arterial hypertension, atrial fibrillation, use of beta-blockers or left ventricular hypertrophy with dynamic obstruction of the left ventricular outflow tract), dipyridamole<sup>8-10</sup> could be an alternative in the preoperative assessment of these patients.

There is no similar study in the literature that comparatively analyzes, in a single center, the results obtained by stress echocardiography with dipyridamole and dobutamine in the preoperative assessment of patients undergoing major vascular surgery.

Our aim was to determine if dipyridamole stress echocardiography can be used as an alternative to dobutamine stress echocardiography in the prognostic stratification of patients who require major vascular surgery.

## PATIENTS AND METHOD

### Study population

A retrospective study was made of 157 patients referred to our laboratory for stress echocardiography (SE) as part of the preoperative studies for vascular surgery. All patients were consecutive and all the stress echocardiographies made for vascular surgery at our center for 2 years are included in this group. Of 157 patients in which preoperative stress echocardiography was performed, 12 (6.9%) did not undergo surgery: in 10 had a poor acoustic window, 1 patient refused, and in

the test was contraindicated in 1. In another 12 patients, the surgical intervention was not carried out, independently of the result of SE: 8 had severely depressed left ventricular systolic function and 4 patients refused. The remaining 133 patients constituted the study population (age 63±11 years and 98% men).

Of the 133 patients in the study, dipyridamole and dobutamine SE were performed in 94 (70.7%) and 39 (29.3%) patients, respectively. The use of one drug or another depended on medical criterion and the clinical characteristics of the patient. The choice of drug was never based on the pretest probability of suffering ischemic heart disease, but on the presence or absence of contraindications for a certain drug. Thus, dobutamine was contraindicated in patients with severe arterial hypertension, atrial fibrillation, use of beta-blockers, and left ventricular hypertrophy with dynamic obstruction of the left ventricular outflow tract. Dipyridamole was contraindicated in cases with severe COPD, severe bradycardia, advanced atrioventricular block, sick sinus syndrome, or cerebrovascular disease.

The assessment parameters were: *a*) change of surgical decision based on the result of the SE, and *b*) cardiac events: cardiovascular death, nonfatal myocardial infarction, coronary revascularization, primary angina, sustained ventricular tachycardia, and ventricular fibrillation.

### Pharmacological protocol

*Dobutamine.* The dobutamine infusion was made through a peripheral vein, beginning with an infusion rate of 10 µg/kg/min and increasing the dose every 3 min by 10 µg/kg/min for a total dose of 40 µg/kg/min. This last stage lasted 6 min. If the test was negative after dobutamine infusion and the patient had not reached 85% of maximum frequency, atropine 1 mg was administered.

*Dipyridamole.* The dipyridamole infusion was made through a peripheral vein, administering a perfusion of 0.84 mg/kg for 6 min and a 1 mg dose of atropine 4 min after concluding perfusion.

### Echocardiographic study

The studies were made with an Agilent Sonos 5500 echocardiograph, using harmonic imaging with transmission and reception frequencies of 1.8 and 3.6 MHz, respectively.

Blood pressure was determined and an electrocardiogram was made at baseline and the end of each stage. The reasons for stopping the test included: development of echocardiographic positivity, reaching 85% of theoretical maximum heart rate, development of progressive angina, severe ventricular arrhythmias, and development of severe hypotension or significant

hypertension.

Images were acquired with the patient in left lateral supine position using standard planes in each patient (longitudinal axis and short parasternal axis, as well as the apical four-chamber and two-chamber section). A specific digital analysis program of stress echocardiography was used. Images obtained at rest, with low doses of medication, at maximum stress, and recovery were stored. The studies were recorded on video and digitized on optical disks in cine-loop format.

Segmental contractility was analyzed using the 16-segment model recommended by the American Society of Echocardiography<sup>11</sup> and each segment was graded on a 4-point scale: 1, normal; 2, hypokinetic; 3, akinetic, and 4, dyskinetic. Ischemia was defined as the appearance of a new disturbance in segmental contractility that was not present in the baseline study and involved at least 2 dependent segments of the same artery. The development of dyskinesia in akinetic segments in the study at rest was not considered ischemia.

### Statistical analysis

Quantitative variables are expressed as mean±standard deviation and qualitative variables as proportions (percentages). The chi-square test was used to compare proportions. The level of statistical significance considered was a value of  $P<.05$ , although values  $<.10$  were also expressed. The positive and negative predictive values of both techniques were calculated for the detection of possible cardiac events during and after surgery.

## RESULTS

### Study group. Clinical characteristics

Our study group was constituted by consecutive patients referred by the vascular surgery department for preoperative study. The mean age of the patients was  $63\pm 11$  years and 98% were men. The choice of drug for SE was based on clinical criteria (in absence of pharmacological contraindications). The stress modality was not chosen in accordance with the possible

prevalence of coronary disease or less favorable clinical profile. In the 133 patients, the incidence of smoking, hypercholesterolemia, history of ischemic heart disease, advanced age, or presence of three or more risk factors was similar in both groups (Table 1). Obviously, since severe hypertension is a contraindication for dobutamine echocardiography, there were fewer hypertensive patients in this group (Table 1). The dipyridamole echocardiography group had a larger number of patients with diabetes mellitus (Table 1).

### Results of stress echocardiography

In patients with both dobutamine as and dipyridamole SE, no complications or symptoms occurred during the test that required the test to be discontinued.

Of the 133 patients studied, SE was positive in 15 (11.3%): 2 (5.1%) of the 39 dobutamine SE and 13 (13.8%) of the dipyridamole SE ( $P=NS$ ). In addition, 8 dobutamine SE (20.5%) were inconclusive because the patient did not reach a heart rate of more than 85% of the maximum expected rate.

The surgical strategy was modified as a result of the SE findings in 9 (6.8%) of the 133 patients (all with positive SE): 2 patients (1.5%) underwent a less aggressive intervention than originally scheduled and 7 patients (5.3%) did not undergo surgery finally. Therefore, 126 of the 133 patients were finally operated. The intervention was carried out for peripheral arterial disease of lower limbs in 62 cases (49.2%), aneurysm of the abdominal aorta in 59 (46.8%), and carotid disease in 5 (4.0%); general anesthesia was used in 102 (81.0%) and epidural or local anesthesia in 24 (19.0%) (Table 2).

Of the 126 patients who underwent surgery, 8 (6.3%) had positive SE (all dipyridamole SE). As mentioned above, in 2 patients the type of intervention scheduled was changed to a less aggressive operation. Another 6 patients with positive SE, of the 126 patients intervened surgically, underwent previous coronariography, which showed that all of them had significant coronary disease. One of these patients underwent revascularization by coronary angioplasty.

TABLE 1. Clinical characteristics of patients undergoing surgery

Risk factors	Dipyridamole SE	Dobutamine SE	P
Arterial hypertension	58%	37.1%	.046
Diabetes mellitus	22.5%	5.7%	.035
Present or previous smoking habit	87.5%	91.4%	NS
Hypercholesterolemia	34.9%	30.3%	NS
Previous CVA	8%	2.9%	NS
History of ischemic heart disease	23.6%	21.6%	NS
Age>70 years	39.3%	37.8%	NS
Three or more factors	59.8%	41.2%	.071

\*Angina, infarction, or previous revascularization. SE indicates stress echocardiography; CVA, cerebrovascular accident; NS, not significant

TABLE 2. Relation between the result of stress echocardiography (SE) and type of intervention

	Lower limbs		Aortic aneurysm		Carotid surgery	Total
	General anesthesia		General anesthesia		General anesthesia	
	Yes	No	Yes	No	No	
Dipyridamole SE	35	9	38	5	2	89
Positive	2	2	4	0	0	8
Negative	33	7	34	5	2	81
Dobutamine SE	13	5	16	0	3	37
Positive	0	0	0	0	0	0
Negative	10	3	14	0	2	29
Inconclusive	3	2	2	0	1	8
Total	48	14	54	5	5	126

TABLE 3. Patients with cardiovascular events

SE	Result of SE	Disease	General anesthesia	Event	No. of risk factors
1 Dipyridamole	Positive	Aortic aneurysm	Yes	Angina (medical treatment)	3
2 Dipyridamole	Negative	Lower limbs	Yes	Angina (medical treatment)	3
3 Dipyridamole	Negative	Lower limbs	Yes	Angina (medical treatment)	2
4 Dobutamine	Negative	Lower limbs	Yes	Non-fatal infarction without Q wave	0
5 Dobutamine	Inconclusive	Lower limbs	Yes	Non-fatal infarction without Q wave	3

Cardiac events occurred in 5 of the 126 patients (4.0%): 2 nonfatal myocardial infarctions without a Q wave and 3 anginas that were controlled with medical treatment. Two patients died after the intervention from non-cardiac causes. Of the 5 events, 2 occurred in patients with negative dipyridamole SE, 1 in a patient with a positive dipyridamole SE, 1 in a patient with negative dobutamine SE, and one in a patient with an inconclusive dobutamine SE (Table 3). Thus, the rate of events was 12.5% (1/8) in patients with positive dipyridamole SE, 2.5% (2/81) in patients with negative dipyridamole SE, 3.5% (1/29) in patients with negative dobutamine SE, and 12.5% (1/8) in patients with an inconclusive dobutamine SE.

Consequently, the negative predictive value of dipyridamole SE and dobutamine SE for the occurrence of cardiac events was 97.5% and 96.5%, respectively.

## DISCUSSION

Risk stratification in patients preparing to undergo major vascular surgery is frequently difficult. Many patients suffer significant coronary disease that is not clinically manifested by the physical inability to exercise. In addition, limitations to physical exercise mean that the stress test is generally not useful in these patients. On the other hand, disturbances in the baseline electrocardiogram (bundle-branch block or left ventricular hypertrophy) are relatively frequent. For all these reasons, pharmacological radionuclide stress tests with isotopes and pharmacological stress echography have

been used for some time.

Stress echocardiography has been shown to have a clear prognostic value in patients undergoing vascular surgery, particularly with dobutamine, but also with dipyridamole. Patients with positive SE have a greater incidence of cardiovascular events, such as cardiac death or nonfatal infarction, in comparison with those with negative SE. The experience of different groups with dobutamine or dipyridamole indicates that these tests have a high negative predictive value, between 90% and 100%. Their positive predictive value is much lower, between 25% and 45%.

In the series of Poldermans et al., the presence of a significant disturbance in parietal mobility in the dobutamine SE was a predictor of risk of perioperative events after multivariate adjustment for different clinical and echocardiographic variables. The same group reported that dobutamine SE is the most powerful predictor of late cardiac events after major vascular surgery and is superior to simple clinical assessment.<sup>16</sup>

Sicari et al.,<sup>18</sup> in the EPIC study of 506 patients assessed with dipyridamole SE before vascular surgery, demonstrated that the sensitivity and specificity of the test for cardiac events were, respectively, 81% and 87%, with a positive predictive value of 28% and a negative predictive value of 99%.

The value of SE in the prognostic assessment of these patients did not differ significantly from that of radionuclide tests. With respect to dipyridamole versus thallium-201, the positive predictive value in studies of more than 100 patients was 4% to 20%, with the nega-

tive predictive value for normal tests reaching 99% for myocardial infarction and/or death. A meta-analysis of 15 studies in which dipyridamole and thallium-201 were compared with dobutamine stress echocardiography for the stratification of perioperative risk demonstrated that both techniques are comparable, although the accuracy varies with the prevalence of coronary artery disease.

Therefore, a positive SE can lead, in itself or after taking into consideration other markers of perioperative risk, to taking measures such as using antianginal drugs like beta-blockers, carrying out more intensive hemodynamic and cardiac monitoring, performing less aggressive surgery, or even canceling or postponing the intervention.

Data comparing the prognostic value of dobutamine SE and dipyridamole SE in patients undergoing vascular surgery is scarce. There has been no prospective study in consecutive patients in which dipyridamole SE and dobutamine SE were performed to compare the alternatives of dipyridamole and dobutamine SE in this type of patients. Our study demonstrated that the negative predictive value for the occurrence of cardiac events was very high for dipyridamole SE (97.5%) as well as for dobutamine SE (96.5%). In our group, patients were not assigned to one modality of SE or another in relation to the pretest probability of suffering ischemic heart disease. What is more, the fact that patients in the dipyridamole group had a less favorable clinical profile only reinforced the hypothesis that this modality of SE is an excellent alternative to dobutamine.

Our results were similar to those obtained in the studies mentioned previously, which used SE to predict perioperative ischemic events in patients undergoing vascular surgery. As far as positive predictive value is concerned, it could not be studied in the case of dobutamine SE because no patient with dobutamine SE finally underwent surgery. With regard to dipyridamole SE, the positive predictive value was apparently low (12.5%) (as reported in the literature), probably due to several reasons: *a*) many patients with positive SE (5 of the 13 patients with positive dipyridamole SE) did not undergo surgery; *b*) in some patients with positive dipyridamole SE ( $n=2$ ), the intervention that was finally performed was less aggressive than the intervention initially scheduled, and *c*) it is likely that all patients with positive SE were subject to more protection and monitoring, in order to reduce the incidence of complications. In any case, we should not forget that SE was carried out for a prognostic rather than a diagnostic purpose and that, therefore, a positive predictive value of 12.5% in this case implies an incidence of cardiac events of 12.5%, which is relatively high. Also, the 12% of events that patients with an inconclusive dobutamine echocardiography suffered should be noted, a finding that should be considered clinically

when assessing this subgroup of patients.

## Study limitations

This study has several limitations. In the first place, many of the patients with a positive SE did not undergo surgery. Nevertheless, this is inevitable in prognostic studies of SE because decision-making is not indifferent to the result of the SE. Secondly, dobutamine and dipyridamole SE were not performed prospectively in the same patients, the populations were different. Although the use of dobutamine or dipyridamole was decided on the basis of characteristics that were not necessarily associated with the prevalence of coronary artery disease, we cannot exclude a selection bias of this type. Nevertheless, we must emphasize two points. On the one hand, that a drug used in SE is generally chosen on the basis of the clinical characteristics of the patient, particularly the potential contraindication of dobutamine or dipyridamole. Consequently, this bias is difficult to avoid. In addition, centering on our population group, the only differences in the risk factors that suggested a pretest probability of suffering ischemic heart disease indicated that the most unfavorable group (more hypertensive and diabetics) was the group in which dipyridamole echocardiography was performed. Nonetheless, the negative predictive value of the dipyridamole SE group was similar to that of dobutamine, reinforcing the idea that dipyridamole SE is a valid alternative to dobutamine in these patients. This study does not contribute information about the sensitivity and specificity of stress echocardiography in diagnosis of ischemic heart disease in this subgroup of population. It must be noted that this was not the aim of the study and that many publications have reported this information. For this reason, it was not considered opportune to perform coronariography or another test in order to calculate the sensitivity and specificity of the test.

Finally, follow-up was restricted to the hospital, so we cannot exclude the possibility that events took place after hospitalization. Nevertheless, since the aim of the study was to analyze the prognostic value of SE in complications associated with vascular surgery, a short follow-up was theoretically appropriate.

## Conclusions and implications of study

In spite of its limitations, this study demonstrated that the negative predictive value of dipyridamole SE was similar to that of dobutamine SE in the presurgical assessment of patients who underwent major vascular surgery. The negative predictive values of both tests were very high. The decision to use one drug or the other in assessing these patients should be conditioned by individual factors and the experience of each center.

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