



Pharmacological Stress Echocardiography at Dobutamine in the Search of Ischemia: Epidemiological, Clinical and Tolerance Profile about 270 Patients

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ABSTRACT

Introduction: Stress echocardiography is considered today as a technique in the non-invasive assessment of coronary artery disease. It can detect anomalies in left ventricular segmental dynamics secondary to the ischemic process with excellent precision. The objective of our study is to determine the epidemiological, clinical, electrical and angiographic profile of patients admitted to our training for exploration and screening of coronary pathology on dobutamine stress echocardiography.

Materials and Methods: This is a retrospective study carried out over a period of 2 years between January 2018 and December 2019 on 270 patients admitted to the service of non-invasive explorations of cardiology B of the Rabat University Hospital for pharmacological stress echocardiography at dobutamine for ischemia or study combined with ischemia and viability research.

Results: The average age of our patients was 61.5. A female predominance was noted, the most common risk factor is high blood pressure, 31.5% were asymptomatic. On examination, 69% achieved 100% of theoretical maximum cardiac frequency and only 13% returned positive. The examination is often well tolerated in 89%. The artery affected by ischemia is often that of the anterior ventricular with a percentage of 46.7%.

Conclusion: Stress echocardiography is a valid method in the non-invasive assessment of coronary artery disease, its tolerance is good and its safety is satisfactory. This study reflects the experience of the cardiology B department. It was able to reassess the diagnostic value of this method and invites to conduct prospective studies for a better approach of its prognostic value.

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I. INTRODUCTION

Stress echocardiography is considered today as a preferred technique in the non-invasive assessment of coronary artery disease. The combination of echocardiography with physical or pharmacological stress makes it possible to detect anomalies in left ventricular segmental dynamics secondary to the ischemic process with excellent precision.

The initiation of the ischemic process is obtained either physiologically by subjecting the patient to controlled

physical exertion, or by pharmacological means. Pharmacological stress involves two main categories of substances: positive inotropic agents on the one hand, represented by dobutamine which we use in the echocardiography laboratory of the cardiology department B of the University Hospital of Rabat and other coronary vasodilators hand, dipyridamole type. Stress echocardiography provides diagnostic accuracy similar to that of scintigraphy or magnetic resonance imaging, but at

considerably lower cost, without impact on the environment and without any biological risk for the patient and the doctor.

The objective of our study is to report our experience, and to specify the epidemiological, clinical, electrical and angiographic profile of the patients admitted for exploration and screening of the coronary pathology with the pharmacological stress echocardiography with dobutamine, and this from of a series of 270 admitted to the cardiology department B and also shed light on the activity of the service in non-invasive exploration based on dobutamine stress echocardiography.

II. MATERIALS AND METHODS

II.1 Patients:

Through a retrospective study, carried out over a period of 2 years, between January 2018 and December 2019, relating to 270 patients admitted to the service of non-invasive explorations of cardiology B at the Rabat University Hospital for pharmacological stress echocardiography with dobutamine at the search for ischemia or ischemia and viability, we collected 424 patients in the service of non-invasive operations for a search for ischemia and / or viability with pharmacological stress echocardiography, including:

- 206 Patients admitted for ischemia testing
 - 154 Patients admitted for viability
 - 64 Patients admitted for research and viability and ischemia
- 270 patients received dobutamine echocardiography for ischemia.

The criteria for inclusion in this study are:

- Patients admitted for pharmacological dobutamine ischemia test.
- Patients admitted for dobutamine pharmacological test for viability and combined ischemia
- Patients over the age of 18.
- Patients with a contraindication to a exercise stress test
- Patients who underwent a stress test which was inconclusive (inability to reach theoretical maximum cardiac frequency), presence of chest pain in the absence of significant ECG changes.

The exclusion criteria in this study are:

- Absence of acoustic window
- Ischemic instability
- Patients with a contraindication to high doses of dobutamine (Tight aortic stenosis, severe left ventricle dysfunction, obstructive cardiomyopathy, severe ventricular and supra ventricular arrhythmia)
- Patients with a contraindication to atropine (glaucoma, prostate adenoma, etc.)
- Patients who have not reached theoretical maximum cardiac frequency (hypothyroidism not treated....)
- Patients under the age of 18.

II.2 Methods:

Method of collecting data from the study population All patients undergoing a stress test (pharmacological or exercise) are listed in a prospective register. Data were collected from hospital patient medical records and the stress echocardiography data register using an operations sheet. This sheet is common for all patients admitted for dobutamine echocardiography. The patients collected were subjected to comprehensive interrogation, clinical examination and close monitoring during the course of the examination and at recovery.

II.3 Technical characteristics of pharmacological stress echocardiography:

The examinations were carried out by trans-thoracic ultrasound (TTE) using a General Electric Vivid 9 and Philips cardiac probe, ultrasound machines equipped with harmonic imaging capabilities. A 5 MHz phased array probe was used. The images were digitized in cine loop and saved for later reading and analysis with echocardiogram synchronization. The segmental movement of the walls was evaluated according to the 17-segment model. The parietal contraction was analyzed visually for each segment individually, taking into account both endocardial excursion and systolic thickening.

II.4 Examination protocol:

II.4.1 Before the exam:

- Verification of the equipment of the ultrasound room and the emergency cart.
- Check that the patient has been fasting for 6 hours
- Verification of the discontinuation of beta blockers, bradycardic calcium channel blocker 48 hours before the examination.
- Calculation of the theoretical maximum cardiac frequency according (TMF) to the following formula : $TMF = 220 - \text{age}$
- Physical preparation of the patient:
 - Make a 12-lead electrocardiogram→
 - Blood pressure measurement on the right arm if possible (leave the cuff in place for the following measurements)→
 - Installation of a venous route→
- Place an Y-shaped electric syringe with Dobutamine and a 5% Glucose serum vein guard, which rinses or accelerates the flow during Atropine or beta-blocker injections
- Psychic preparation of the patient

II.4.2 Procedure and monitoring during the examination

Monitoring of symptoms, hemodynamics, electrical and ultrasound is done continuously from the basal state at the end of the infusion, then during the recovery period. The digital acquisition of the image loops in the 4 usual incidences is made at each level: para-sternal short axis cut, apical cut 4 cavities, cut 2 cavities and apical cut 3 cavities.

II.4.3 Landings:

- At each level
 - 12-lead electro-cardiographic tracing→
 - Blood pressure measurement→
 - Echo-cardiographic acquisitions in the 4 aforementioned incidences→
 - Note the various events observed on the monitoring sheet.→
- A continuous infusion in progressive doses of 5, 10, 20, 30, 40 (or even 50 gamma / kg / minute if not removed) for the diagnosis of ischemia
- An intravenous administration of atropine 0.25mg can be useful from 30gamma / kg/min to reach TMF

II.4.4 Calculation of the infusion rate:

For a Dobutamine syringe of 50mg / 10cc, 100mg / 20cc, 250mg / 50cc

(Concentration allowing a quick calculation) 5 gamma / kg / min gives the following flow calculation:

Patient weight x 60/1000 = ml / h

II.4.5 The stopping criteria are:

- Achievement of 85% of MTF or 100% if good tolerance knowing that the goal is to reach at least 85% so that the examination is meaningful and therefore interpretable
- Severe atrial or ventricular rhythm disturbances
- Increase in systolic pressure over 230mmHg and diastolic over 140mmHg
- Symptomatic hypotension
- Sinus bradycardia or conductive block
- Left intraventricular obstruction
- ECG modification (ST segment over / under offset > 2mm)

II.4.6 After stopping:

The half-life of dobutamine is 3 minutes:

- Monitoring of blood pressure for 6 min until returning to the starting figures
- Echo-cardiographic monitoring of possible changes in kinetics
- Recording of an electrocardiogram after 6 min, then the patient will be perfused and released from the electrodes

II.5 Statistical method

The data collected was then the subject of a statistical study which was conducted by Excel software.

III. RESULTS

A. Epidemiological data:

1. Prevalence:

During a period of 2 years, from January 2018 to December 2019, the cardiology B department admitted 424 patients to the non-invasive exploration service for a search for ischemia and / or viability on pharmacological stress ultrasound. , whose:

- 206 patients admitted for ischemia research
 - 154 patients admitted for viability
 - 64 patients admitted for viability and ischemia research
- Thus, 270 patients benefited from a dobutamine echocardiography in search of ischemia, or 63%

2. Age:

The age of our patients is between 34 and 83 years with an average of 61.5 years.

3. Sex:

There is a slight female predominance at 51% versus 49% for men.

4. Cardiovascular risk factors:

In this series, 49 patients or 18% had no cardiovascular risk factor.

Hypertension was the leader with 60% followed by diabetes with 33%. Smoking and dyslipidemia were present in 27% and 23% of patients, respectively

B. History:

- One patient had a history of ischemic stroke, 6 others were chronic hemodialysis, and 3 patients are followed for obliterating arterial disease of the lower limbs
- Ischemic heart disease was found in 90 patients or 33% of the study population.
 - Coronary angiography was performed in 60%
 - Endovascular revascularization was performed in 51% of patients who underwent angiographic exploration
- 3 patients had a coronary artery bypass history.

C. Clinical profile:

Asymptomatic patients were referred for a stress examination for multiple reasons:

- Pre-operative screening for non-cardiac surgery (vascular, visceral, traumatology)
- Screening in diabetic patients
- Assessment of documented ischemic heart disease unexplored angiographically in patients remaining asymptomatic
- Evaluation of an ischemic heart disease documented and explored angiographically, and having pluri-truncular and / or intermediate lesions in patients remaining asymptomatic

In our study, 68.5% of patients were symptomatic, compared to 31.5% asymptomatic. The clinical picture was mainly dominated by atypical angina and exercise angina with 40.5% and 28% respectively. Angina at rest and dyspnea ranked second with 15% and 10.5%. Mixed angina represented only 5%.

D. Electrical profile:

1. Basic state :

60% of patients had a normal baseline electrocardiogram at admission while 40% had electrical abnormalities.

2. Abnormal basic electrocardiogram:

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The electrical anomalies were distributed as follows:

- 46% negative T waves
- Q wave of necrosis in 45%
- Surelevation of ST / Left branch block at 8%

E. The dobutamine protocol:

1. The dose administered during the examination:

61% of the study population had received 40 gamma, while 32% had received 30 gamma. The 20 gamma dose was administered to only 4% of patients, while no one had less than 20 gamma

2. The maximum frequency reached

In this series, 69% of patients were able to reach 100% of TMF. 30% achieved an TMF value between 85% and 100% while the remaining 6% reached 85%.

3. Atropine

During the protocol, doses of atropine were administered. 70% received more than 1mg of atropine

F. Echo-cardiographic data:

1. In the basic state

84 patients had kinetic disorders at baseline, or 31%, this because we included patients admitted for viability and ischemia research

2. The territories where kinetic disorders occur in the basic state: are

- Interventricular artery: 32.9%
- Circunflex artery: 9.8%
- Right coronary: 11.6%
- Interventricular artery / Circunflex artery: 22.8%
- Circunflex artery / Right coronary: 15.7%
- Interventricular artery / Circunflex artery / Right coronary : 6.9%

G. Ischemia test result:

The ischemia test was positive in 13% of patients and negative in 86% of cases.

1. Ischemia test positivity threshold 68.5% of the effective tests were positive during the peak of the examination, 26.5% at low dose and 4.5% during the recovery.

2. The areas of positivity of the ischemia test: The territories concerned were:

- Interventricular artery: 46.7%
- Circunflex artery: 25.8%
- Right coronary: 8%
- Interventricular artery / Circunflex artery: 10.5%
- Circunflex artery / Right coronary: 4%
- Interventricular artery / Right coronary / Circunflex artery: 5%

3. Epidemiological profile of patients with positive ischemia

- The sub-population; positive test; is made up of 54% women and 46% men.

- The risk factors found:

- hypertension present in 45% of patients
- Diabetes in 42% of cases
- Smoking in 40%
- Dyslipidemia in 20%

- 45% of these patients had ischemic heart disease as history
- 68% with a positive ischemia test were symptomatic and 42% had an angina

4. Undesirable effects:

The undesirable effects occurred in 11% of the study population.

Among the rythm disturbances:

- 2 patients presented with sustained ventricular tachycardia
- 2 cases of unsupported ventricular tachycardia
- 2 cases of supra-ventricular tachycardia
- 12 cases presented with ventricular extrasystoles

Conductive disorders:

- 1 patient presented a 1st degree auriculo-ventricular block at the peak of the stress test, which regressed on recovery
- Chronotropic insufficiency has been suspected in a patient with goiter not followed

IV. DISCUSSION

1. Epidemiological data:

The table below summarizes the main epidemiological results from clinical studies on stress echocardiography. Note that these were performed on a larger number of patients (1, 2, 3).

Epidemiological characteristic	Chuah et al (1998)	Argarwal et al. (2016)	Gurunathan et al. (2017)	Our series (2019)
Number of patients	860	225	374	270
Avrage age	70	65	83	61.5
male (%)	55.7	37	46	51

The predominance of women has been widely reported in the literature, this same finding was found in our series and this can be explained by the atypical clinical presentation of ischemic pathology in women requiring non-invasive

explorations, as well as the interest of stress echocardiography and its contribution in this category compared to the stress test.

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2. Clinical data:

Hypertension was the main risk factor reported in our series (60%), this result was found in other authors with a

homogeneous distribution of other cardiovascular risk factors (4,5).

Cardiovascular risk factors	Chuah et al (1998)	Argarwal et al. (2016)	Gurunathan et al. (2017)	Our series (2019)
Hypertension	63%	43.7%	84%	60%
Diabetes	26%	17.3%	19.2%	33%
Dyslipidemia	62%	22.6%	78.1%	27%
Smoking	20%	5.6%	18.5%	23%

Among the patients with a positive test, the hypertensive profile was predominant in our study, followed by diabetes

and smoking with 45%, 42% and 40% respectively. In Gurunathan's series, smoking only represented 12% (2)

Cardiovascular risk factors in patients with a positive test	Gurunathan et al. (2017)	Our series (2019)
Male	45%	46%
Hypertension	83%	45%
Diabetes	31%	42%
Smoking	12%	40%
Dyslipidemia	77%	20%

The reason for requesting a stress echocardiography is variable. The discovery of an ischemic heart disease can be fortuitous during the performance of a stress examination in an asymptomatic patient sent as part of screening for diabetic patients, in a preoperative assessment for non-cardiac surgery, for evaluation of a known or even revascularized coronary artery disease or in front of intermediate lesions in coronary angiography. 31.5% of the patients in our series were asymptomatic. Our result is more

important than that reported in the literature at around 10% (2)

In symptomatic patients, the functional signs are often specific and guiding. It may be effort dyspnea related to heart failure complicating silent ischemic heart disease, or atypical chest pain as in our experience where 40.5% of the symptoms reported was atypical chest pain, and dyspnea at 10.5%

Clinical features	Chuah et al	Gurunathan et al.	Agarwal et al.	Notre série
Chest pain	26%	66%	37%	88.5%
Dyspnea	17%	19%	21%	10.5%

3. Protocol and results:

Baseline echocardiography objectified kinetic anomalies in 31%, this percentage is much higher than that found in the literature. Gurunathan et al. reported a result of 17% and the series by Kim et al. 19%. This difference in outcome can be explained by the fact that our study included patients admitted for concomitant research into ischemia and viability. (2,5)

The average dose of dobutamine used according to the authors is 37.7ug / kg / min (2,3,5).

The same result was found in our series.

Achieving 100% TMF is rarely associated with maximum dose use of dobutamine. In a study involving only patients who received high doses of dobutamine, the average TMF was 80%. In our series 61% of patients received 40ug / kg / min of dobutamine and 69% reached 100% of TMF. This difference is explained by the exclusion criteria used in our

study where sub-maximal stress echocardiograms were excluded from the study. (6)

Co-administration of atropine is a safe and effective strategy in patients with an inadequate chronotropic response. If 85% of the TMF was not reached, atropine was administered at a rate of 0.25 mg / min to a maximum of 2 mg while maintaining the continuous infusion of dobutamine. Recently, new protocols have been developed, including the early injection of atropine at a dose of 20ug / kg / min when the heart rate is less than 100b / min.

Early injection of atropine during dobutamine stress echo reduced the duration and dose of dobutamine infusion, as well as the side effects of dobutamine, while maintaining similar diagnostic accuracy .

In our study, we used the early atropine protocol. In order to reach TMF we used physical effort in synergy. This practice

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is recommended in literature through an isometric exercise using a foam ball tight in the hand.

Detection of ischemia was positive in 13% of our series. Similar results have been reported in the literature.

Result of stress echocardiography	Chuah et al	Gurunathan et al.	Kim et al.	Notre série
Positive ischemia	65%	13%	22.8%	13%

4. Tolerance and side effects:

The occurrence of life-threatening complications is rare. Data from the International Register of Stress Echo Complications report a rate of 1 in 6,574 patients undergoing physical stress echocardiography and 1 in 557 patients undergoing dobutamine echocardiography. (7) In our study, no deaths, myocardial infarctions, ventricular fibrillation or severe conduction disorders were observed. Several studies have reported an incidence of 0.002%, 0.02%, 0.04% and 0.23% respectively with the use of dobutamine as a stressor. (8)

We recorded 2 cases of sustained ventricular tachycardia, or 0.7%. The reported incidence is 0.15%.

The clinical significance of ventricular tachycardia induced by dobutamine stress echo has not been clarified. Previous studies (9,10) have failed to establish a relationship between this ventricular rhythm disorder and induced myocardial ischemia. Elhendy et al. (11), out of a series of 286 patients who underwent a dobutamine stress ultrasound were not predicted by the presence or extent of coronary artery disease or by the induction of ischemia during echo of stress. Although the administration of intravenous beta-blockers is routine in dobutamine echocardiography protocols at a dose of 1 mg up to 5 mg / 5 min, this data was not mentioned in our registry and has not could be exploited. This injection authorizes the patient to resume oral treatment

with the usual beta-blockers in order to ensure protection at the end of the action period of the injected beta-blocker.

The arrhythmia observed can be attributed to stimulation of beta-1 receptors, reduction of dobutamine-induced ventricular refractory period (12), or reduction of dobutamine-induced plasma potassium (13).

Severe hypotension occurred in 0.7%, the reported incidence being 20% (8). Although the hypotensive response during physical exercise has been strongly associated with myocardial ischemia and poor cardiac prognosis, hypotension during dobutamine infusion cannot be considered a specific indicator of cardiac abnormalities (14). The mechanism of the hypotensive response during the dobutamine infusion remains unclear. Vigorous contraction of the myocardium around a small chamber can trigger sympatho-inhibition and increased parasympathetic flow, leading to systemic hypotension (15). The prognostic significance has been widely discussed, most studies have not reported any significant association with the occurrence of cardiac complications, while Dunkelgrun et al. in a retrospective study of 3381 patients showed that severe hypotension during the dobutamine infusion is an independent predictor of cardiac death and non-fatal myocardial infarction (16)

The table below represents the main side effects reported in the literature (17)

Undesirable effects	Pellikka et al.	Seknus et Marwick	Picano et al.	Kim et al.	Chuah et al.	Our séries
Myocardial infarctions	0.1%	0.03%	0.06%	-----	0%	0%
Ventricular tachycardia	0.4%	0.16%	0.06%	0.9%	2.4%	0.7%
Ventricular fibrillation	0%	0%	0.06%	-----	-----	0%
Hypotension	0%	0.03%	0.03%	-----	3.2%	0.7%
Nausea	-----	-----	-----	3.4%	8%	2.2%

V.CONCLUSION

Stress echocardiography is a valid method for the non-invasive evaluation of different expressions of coronary artery disease. We wanted to critically review the results of our experience with regard to the epidemiological and clinical profile as well as the indications, results and tolerance. Our results can be superimposed on those of the literature. Tolerance is good and its safety is satisfactory.

One of the obstacles to wider dissemination of this technique is the pro-arrhythmogenic reputation induced by the infusion of dobutamine in high doses. This study reflects the experience of the cardiology department B without claiming to reassess the diagnostic value of this method and encourages the conduct of prospective studies for a better approach to its prognostic value.

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