Safety and Feasibility of Dobutamine-Atropine Stress Echocardiography in Octogenarian Patients

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Objective

To assess the feasibility and safety of dobutamine-atropine stress echocardiography (DASE) in octogenarians.

Methods

We evaluated 5,467 DASE which were distributed in two groups: group I (GI) with 203 DASE performed in octogenarians, and group II (GII), the control group, with 5,264 DASE. The mean age of GI and GII was 83±3 (80-95) and 59±11 (17-79) years, respectively. DASE parameters that were prospectively collected, were compared and analyzed.

Results

The percentage of patients that achieved maximum heart rate was 63.5% in GI and 41% in GII (p<0.001), and GI patients required less atropine compared to GII (GI=47%, GII=78%, p<0.001).The presence of chest pain (GI=13%, GII=15.6%, p=0.429) and DASE positive for myocardial ischemia (GI=20.7%, GII=16.9%, p=0.296) were not statistically different between the two groups. However, concomitant positive DASE and absence of chest pain (GI=17%, GII=11%, p=0.029) was higher in GI. The incidence of premature beats in GI was higher than in GII (GI=47.8%, GII=27.6%, p<0.001), and there were more supraventricular tachyarrhythmias (ST) in GI than in GII (GI=5.9%, GII=1.9%, p=0.001). Out of 11 ST that happened in GI, 9 reverted spontaneously. There weren't either deaths or acute myocardial infarction. Ventricular fibrillation only happened in GII (2 cases, 0.03%).

Conclusion

In the present study, octogenarians achieved maximum heart rate more frequently despite the lesser amount of atropine that they required for DASE completion. Moreover, in this elderly population, there was a higher correlation between positive DASE and absence of chest pain. Although octogenarians did present more heart rhythm disturbs, they usually resolved spontaneously. In our study, DASE proved to be feasible and safe in octogenarians.

Key words

echocardiography, dobutamine, octogenarian

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Received on 10/17/04 • Accepted on 03/04/05

Since stress echocardiography with physical exercise was started by Wann[1], and dobutamine was used as cardiac stress stimulator by Mason[2], important technological advancements with image digitalization and distinctive study protocols have been developed[3,4]. That allowed for, both on hospital and ambulatory[5-7] level, echocardiography became as effective and safe method for myocardial ischemia diagnosis, as nuclear medicine[8-10].

The inability of an individual exercise properly and unsatisfactory electrocardiographic records can reduce the precision of a supplementary method in myocardial ischemia research, especially among elderly patients, which could favor the use of a pharmacological stress stimulator[11,12].

Octogenarians constitute a population with higher probability of coronary artery disease (CAD). However, the lack of classic anginous symptomatology may be related to physical activity decrease at the extent in which ischemic symptoms are not present, and the fact that many elderly individuals do not achieve sub-maximum heart rate (HR)[13] is relevant.

A greater incidence of atrial fibrillation[14] and ventricular arrhythmia[15] takes place among octogenarian patients than among young ones. Besides, elderly patients, when submitted to dobutamine-atropine stress echocardiogram (DASE), show more ventricular arrhythmia, more hypotension and lesser angina manifestation than in younger population[16], which can make them more susceptible to complications or determine exam interruption. Another significant aspect is that, among octogenarians, a greater incidence of prostatic symptoms is seen, which can be associated to acute urinary retention[17] and under that condition, prostatism may make the use of atropine during dobutamine stress echocardiogram not feasible and compromise the efficiency of the method.

By having in view possible advantages, limitations and risks of a pharmacological stress stimulator in elderly individuals, we aimed at verifying the safety and feasibility of DASE in octogenarian patients.

Methods

A prospective collected database of probable or known DAC patients, who had been submitted to DASE, was retrospectively assessed. In the period from July 1996 to December 2003, 5,467 DASE were carried out in 4,997 patients, who were sent, at clinical cardiologist discretion, to our echocardiography service, set up in a cardiological emergency care hospital.

We guided all patients to be submitted to an ophthalmologic assessment, aiming the possible use of atropine, and suspended β-blockers and calcium antagonists (verapamil or diltiazem) in the period from 24 to 48 hours prior to exam, except in those cases in which the assistant physician requested treatment maintenance.

Through clinical and laboratorial exams or verbal information, the presence of systemic blood pressure (SBP), diabetes mellitus (DM), dyslipidemia (DLP), family history for DAC, smoking, known DAC, myocardial revascularization through surgery (SMR) or through transluminal angioplasty (TLA) was investigated.

SH was considered when blood pressure (BP) at rest has higher than or equal to 140 x 90 mmHg; DM, when fasting glycemia was higher than 140 mg/dl; DLP, when total cholesterol was greater than 200 mg/dl. SH, DM and DLP diagnoses were also taken into consideration if the patient was under use of BP, glycemia or cholesterol reducing medication, respectively.

We clarified on the risks and objectives of exam, more frequent dobutamine and atropine side effects and, only after verbal agreement from the patient, DASE was started.

Octogenarians group I (GI), with average age of 83±3 (80 to 95) years old, amounting 192 patients, with 203 exams; and group II (GII), the control group, with average age of 59±11 (17 to 79) years old, in a total of 4,805 patients, with 5,264 exams, were considered.

Dobutamine was used in doses of 5, 10, 20, 30 and 40 μg. Kg-1. min-1 in 3-minute intervals, with the aim of achieving at least 85% of maximum heart rate (HR) (220 minus the age in years old) and/or determining contractile abnormality compatible with myocardial ischemia. Atropine was started in the third or fourth stage, if HR was lower than 100 bpm; or if target HR was not achieved in the fourth stage of dobutamine, since contractility worsening or new contractile abnormality had not taken place[18-20]. Atropine dose varied from 0.25 mg to 2 mg. In patients who showed ischemia, 5 to 10 mg of endovenous de metoprolol were administrated.

BP was measured at the beginning of each stage and at the end of the exam. Electrocardiographic monitoring was continuous and twelve-derivation electrocardiogram was carried out before the beginning of and at DASE completion. DASE conclusion was considered in cases with ischemia-compatible contractile abnormality and/or 85% of maximum heart rate was achieved, except in myocardial viability assessment.

Equipment used (Apogee CX 200 and Vingmed System Five) allowed for the use of quad screen, in such way that all four stages could be side-by-side displayed for analysis, by viewing the heart on paraesternal (long and short axis) and apical (four and two cameras) levels. All exams were recorded in videotape and, part of them (positive for), also in optic disk.

All DASEs were carried out by two echocardiographers (simultaneously) and the interpretation (through consensus) was done immediately after exam completion. Left ventricle was divided in sixteen segments, with wall contraction classified as normal, hypokinetic, akinetic, dyskinetic or aneurysmatic, according to American Society of Echocardiography[21].

Thoracic pain, when present, was considered as typical or atypical.

Hypertensive peak was defined when BP was greater than or equal to 230 x 120 mmHg, and hypotension was considered when systolic blood pressure (SBP) decreased in 20 mmHg or when SBP was lower than 100 mmHg. It was also verified the possible occurrence of extra-systole with less than three consecutive heartbeats (ES), supraventricular tachyarrhythmia (SVTA), in which atrial tachycardia, supraventricular paroxystic tachycardia, fibrillation and atrial flutter; sustained ventricular tachycardia with duration >30 seconds (SVT), non-sustained ventricular tachycardia (NSVT), ventricular fibrillation (VF), acute myocardial infarction (AMI) and death were included. Even with no completion, DASE should be interrupted in the presence of hypertensive peak, symptomatic hypotension, SVTA, SVT, NSVT, VF, or by request from the patient.

Descriptive analysis was carried out when, for continuous variables, means plus or minus a standard deviation were calculated. For association analysis between categorical variables, chi-square test of Pearson, verisimilitude rate test and exact test of Fisher were applied. When there was association between categorical variables, to measure association level, odds ratio estimate and confidence intervals of 95% were used. In continuous variable assessment, continuous variable normality test was carried out through Kolgomorov-Smirnov test. For data normality, mean comparison test was carried out through t-test of Student for independent populations. For continuous variables, whose distribution was not normal, Mann-Whitney non-parametric test was employed for comparison of two means.

Results

From the total of 5,467 exams, 5,189 diagnostic exams were obtained, being 934 (18%) from those exams, positive diagnostic tests for myocardial ischemia; 4,153 (80%) negative and 102 (2%) carried out to examine myocardial viability. Among all exams, 278 (5%) of them were non-conclusive.

As evidenced in comparative analysis (tab. I), between octogenarian patient group (GI) and control group (GII), there is a prevalence of female sex individuals in GI (58%) and GII (56%), but without significance (p=0.565). Octogenarians showed more occurrence of maximum HR than control group individuals (63.5% vs. 41.2%, p<0.001) and there was no significant there was no significant difference between positive (20.7% vs. 16.9%), negative (73.9% vs. 76%) tests, for viability (1.5% vs. 1.9%) and non-conclusive (3.9% vs. 5.1%) tests of groups I and II, respectively. Prevalence of typical chest pain (6.4% vs. 9.6%), atypical pain (6.9% vs. 6%) or any other one (13.3% vs. 15.6%) did not allow for a distinction (p=NS) between the two groups. GI used less atropine (47.3% vs. 78.1%, p<0.001) and showed more ES (47.8% vs. 27.6%, p<0.001) and SVTA (5.9% vs. 1.9%, p<0.001) than GII. NSVT occurrence (0.5% vs. 0.2%) was not different (p=NS) between both groups, and the two VF cases recorded occurred in group control. There was no AMI, SVT or death in the population of this study.

When we assessed the subgroup of octogenarians who had showed positive tests (tab. II), we did not observe correlation (p=NS) with maximum HR and sub-maximum HR. Concerning chest pain, we observed a significant correlation between positive test and

Table I - Comparative assessment between groups

Parameters	Group I	Group II	p	OR	CI 95% for OR	
Average age (years old)	83±3	59±11				
	N° (%)	N° (%)			LL	UL
Patients	203 (100)	5,264 (100)				
Female sex	118 (58.1)	2,948 (56.0)	0.565			
Maximum HR	129 (63.5)	2,711 (41.2)	<0.001	2.484	1.856	3.323
Sub-maximum HR	56 (27.6)	2,536 (48.2)	<0.001	0.410	0.300	0.560
Test						
Positive	42 (20.7)	892 (16.9)	0.296			
Negative	150 (73.9)	4,003 (76.0)				
Non-conclusive	8 (3.9)	270 (5.1)				
Viability	3 (1.5)	99 (1.9)				
Used atropine	96 (47.3)	4,109 (78.1)	<0.001	0.252	0.190	0.335
Typical chest pain	13 (6.4)	504 (9.6)	0.143			
Atypical chest pain	14 (6.9)	316 (6.0)	0.549			
Chest pain (typical/atypical)	27 (13.3)	820 (15.6)	0.429			
ES	97 (47.8)	1,454 (27.6)	<0.001	2.398	1.809	3.179
SVTA	12 (5.9)	98 (1.9)	0.001	3.312	1.788	6.136
NSVT	1 (0.5)	8 (0.2)	0.289			
VF	-	2 (0.03)	-			

GI - octogenarian patient group; GII - control group; HR - heart rate; ES - extra-systole; SVTA - supraventricular tachyarrhythmia; NSVT - non-sustained ven--tricular ta-chycardia; VF- ventricular fibrillation; OR- odds ratio; CI- confidence interval; LL- lower limit; UL- upper limit. Data displayed as mean±stan-dar-d- de--viation and per-centage.

Table II - Association between positive tests. heart rate and chest pain in the octogenarian patient group

Parameters		Result from Positive Test	p	OR	CI 95% for OR LL	UL
Maximum heart rate						
Present	Nº (%)	28 (21.7)	0.720			
Absent	Nº (%)	14 (18.9)				
Sub-maximum heart rate						
Present	Nº (%)	9 (16.1)	0.438			
Absent	Nº (%)	33 (22.4)				
Typical chest pain						
Yes	Nº (%)	7 (53.8)	0.007	5.167	1.635	16.325
No	Nº (%)	35 (18.4)		1.000		
Atypical chest pain						
Yes	Nº (%)	5 (35.7)	0.172			
No	Nº (%)	37 (19.6)				
Chest pain (atypical/typical)						
Yes	Nº (%)	12 (44.4)	0.003	3.893	1.656	9.152
No	Nº (%)	30 (17.0)		1.000		

Parameters in absolute and percentage numbers; OD - odds ratio; CI - confidence interval; LL - lower limit; UL - upper limit.

Table III - Association between positive tests. heart rate and chest pain in the control group

Parameters		Result from Positive Test	p	OR	CI 95% for OR LL	UL
Maximum heart rate						
Present	Nº (%)	355 (16.4)	0.351			
Absent	Nº (%)	537 (17.4)				
Sub-maximum heart rate						
Present	Nº (%)	416 (16.4)	0.321			
Absent	Nº (%)	476 (17.4)				
Typical chest pain						
Yes	Nº (%)	331 (65.7)	<0.001	14.321	11.679	17.56
No	Nº (%)	561 (11.8)		1.000		
Atypical chest pain						
Yes	Nº (%)	57 (18.0)	0.588			
No	Nº (%)	835 (16.9)				
Chest pain (atypical/typical)						
Yes	Nº (%)	388 (47.3)	<0.001	7.021	5.95	8.285
No	Nº (%)	504 (11.3)		1.000		

Parameters in absolute numbers and percentages; OD - odds ratio; CI - confidence interval; LL - lower limit; UL - upper limit.

occurrence of typical chest pain (53.8% vs. 18.4%, p=0.007) or any other pain (44.4% vs. 17%, p=0.003).

Control group positive test subgroup (tab. III) showed similar behavior to octogenarian subgroup, without correlation (p=NS) between positive test and HR (maximum or sub-maximum). However, there was significant correlation with typical chest pain (65.7% vs. 11.8%, p<0.001) or any other pain (47.3% vs. 11.3%, p<0.001).

When comparing those two subgroups with positive tests (tab. IV), results were not different when maximum HR, sub-maximum HR, presence of any pain, typical or atypical chest pain were considered. However, when considering the absence of typical chest pain (18.4% vs. 11.8%, p=0.009) or the absence of any pain (17% vs. 11.3%, p=0.029), the correlation with octogenarian individual subgroup with positive tests was significantly greater.

We already reported that, in general estimate, octogenarians needed less atropine. Besides, the percentage of patients that achieved maximum HR (tables V and VI) was higher in group I when atropine was administrated (79.2% vs. 45.9%, p<0.001) and also when it was not (49.5% vs. 24.8%, p<0.001).

In specific octogenarian analysis (tables VII and VIII), a (non-significant) predominance of female sex, hypertensive, dyslipidemic women, and those submitted to coronary angioplasty was observed, but only CAD family history and number of diabetic patients were significant (p<0.05) among women. Surgical myocardial revascularization was more frequent among men (p<0.05). In the comparison between patients of both sexes, there was no significant difference between results from DASE concerning the presence of typical or atypical thoracic pain. Systolic blood pressure was no different between sexes and HR among women was higher in DASE at rest and in its peak (p<0.05). Among the 22 (11%) octogenarians who showed hypotension, 14 (64%) were of female sex, with only one symptomatic case taking place. Only one patient had hypertensive peak, however, the exam was completed. Concerning rhythm disturbances, values were not significantly different.

Table IV - Comparison between subgroups of positive test patients: association with maximum or sub-maximum heart rate. chest pain presence or absence

	Group I N° (%)	Group II N° (%)	p	OR	CI 95% for OR LL	UL
Maximum HR	28 (21.7)	355 (16.4)	0.115			
Sub-maximum HR	9 (16.1)	416 (16.4)	1.000			
Typical chest pain	7 (53.8)	331 (65.7)	0.388			
Atypical chest pain	5 (35.7)	57 (18)	0.151			
Chest pain (typical or atypical)	12 (44.4)	388 (47.3)	0.846			
Absent typical chest pain	35 (18.4)	561 (11.8)	0.009	1.690	1.159	2.465
Absent (typical or atypical) chest pain	30 (17)	504 (11.3)	0.029	1.606	1.073	2.405

HR - heart rate; GI - octogenarian patient group. and GII - control group; OR - odds ratio. CI - confidence interval; LL - lower limit; UL - upper limit.

Table V - Comparison between groups: occurrence of maximum heart rate with and without atropine use

Parameters		Maximum heart rate GI	GII	p	OR	CI 95% for OR LL	UL
With atropine	Nº (%)	76 (79.2)	1,884 (45.9)	<0.001	4.488 1.000	2.732	7.372
Without atropine	Nº (%)	53 (49.5)	287 (24.8)	<0.001	2.968 1.000	1.986	4.436

Parameters in absolute numbers and percentages; OD - odds ratio; CI - confidence interval; LL - lower limit; UL - upper limit.

However, there was a higher percentage of ES among men (61%) than in women. Four SVTA occurred in men and seven in women.

The dose used and the percentage of octogenarian women who needed atropine (tab. VI) were lower than those of men ($p<0.05$).

Discussion

Since the use of dobutamine was utilized by Mason[2] as a stress stimulator, in 1984, different works have shown DASE safety in large population[6-8,22]. However, as we have knowledge on, only one article mentions DASE in octogenarians, by analyzing, in a small sample, its prognostic value[23]. Due to their greater tendency for DAC, rhythm disturbances and hypotension, it has become interesting verify DASE feasibility in such high age range.

Secnus and Marwick[24] had already examined that women showed higher HR than men, both at rest and at the end of DASE, and that a lower number of women needed atropine. Besides, Hiro et al.[16] observed that women needed a lower amount atropine. Those two peculiarities[16,24] occurred with octogenarians. Despite achieving more maximum HR than control group, octogenarian individuals (especially women) needed less atropine, which may be due to a lower vagal activity and/or a greater sensitivity to dobutamine, as octogenarians achieved more maximum HR than control group when the two groups used atropine and when they did. As well as verified by Hiro et al.[16] in the assessment of their high age range population (>75 years old), we also observed a greater correlation between absence of chest pain and positive DASE for ischemia among octogenarians, a fact that suggests a decrease of painful sensitivity in that age range.

In studies published by Mertes et al.[22], Elhendy et al.[25] and Poldermans et al.[26] correlation between atropine use and arrhythmia occurrence was not observed, but correlation between tachyarrhythmias and ventricular dysfunction at rest was recorded. Octogenarians from our study had more arrhythmia, although they had used lesser atropine than the other group. Only one octogenarian

Table VI - Use of atropine

Patients	Group I N° (%)	Group II N° (%)	p
Total	96 (47)	4,109 (78)	< 0.05
Male	55 (28.6)		
Female	41 (21)		
Dose	mg	mg	
Total	0.47±0.3	0.71±0.31	< 0.001
Male	0.54±0.36		< 0.05 †
Female	0.41±0.25		

Data expressed in absolute numbers and percentages. and atropine doses expressed in milligrams (mg); GI - octogenarian patient group; GII - control group. † p<0.05 comparing atropine dose used by male and fe-male sex individuals in group I.

Table VII - Analysis of risk factors among octogenarian individuals

	Men N° (%)	Women N° (%)	p
Patients	80 (42)	112 (58)	NS
Hypertension	32 (40)	57 (51)	NS
Diabetes mellitus	6 (7.5)	22 (19.6)	< 0.05
Dyslipidemia	14 (17.5)	33 (29.5)	NS
Family history	5 (6.3)	18 (16.1)	< 0.05
Surgical myocardial revascularization	17 (21.3)	9 (8)	< 0.05
Coronary angioplasty	3 (3.8)	9 (8)	NS

Data expressed in absolute numbers and percentages; NS - non-significant.

Table VIII - Analysis of dobutamine-atropine stress echocardiogram of octogenarian individuals

Test results	Men N° (%)	Women N° (%)	Total N° (%)	p
Positive	18 (22.5)	20 (17.9)	38 (19.8)	NS
Negative	55 (68.8)	88 (78.6)	143 (74.5)	NS
Non-conclusive	7 (8.8)	4 (3.6)	11 (5.7)	NS
Chest pain (typical and atypical)	13 (15)	14 (12)	27 (13.3)	NS
Typical	7 (8.2)	6 (5)	13 (6.4)	NS
Atypical	6 (7.1)	8 (6.8)	14 (6.9)	NS
Hemodynamic parameters				
Systolic BP (rest) mmHg	136	143		NS
Systolic BP (stress) mmHg	149	145		NS
Diastolic BP (rest) mmHg	82	81		NS
Diastolic BP (stress) mmHg	75	71		< 0.05
HR (rest) bpm	72	76		< 0.05
HR (stress) bpm	130	134		< 0.05
Number of patients with hypotension	8	14		NS

BP - blood pressure; HR - heart rate; NS - non-significant.

individual with SVTA had (discreet) contractile abnormality com TASV at rest. Atropine was more often used than the one mentioned in referenced articles, by believing that was possible to increase the number of diagnostic exams, decrease sinus deceleration and prevent from transitory atrioventricular block[18-20,27-29], since that the intoxication possibility is very reduced when the dose does not exceed 2 mg[30]. The fact of not having had acute urinary retention among octogenarians was attributed to the need for using less atropine and that some of them are prostatectomized patients.

Between the two groups there was no significant prevalence of sex, of completed and non-completed tests, nor the occurrence of any kind of pain, even when they were related to positive tests.

Hypotension during DASE has many mechanisms[31-37], however, it is usually asymptomatic, which was also observed in 22 (11%) octogenarian individual hypotension-related DASE, from which the only symptomatic case was the one of a patient with positive DASE for myocardial ischemia. Only one octogenarian showed hypertensive response[38], but the exam was completed. DASE complications, such as asystolia[39], VF or AMI[6,8,40,41] and cardiac rupture[42,43] are rare excerpts from literature, being as infrequent as complications that occur during exercise stress test[44]. There was no SVT, VF, AMI or death in octogenarian group.

Group I extra-systole and SVTA were more frequent, but not determinant for the non-diagnostic tests. From the twelve complex arrhythmias among octogenarians (11 SVTA and 1 NSVT), ten spontaneously reverted; the other two reverted with endovenous amiodarone (one at exam room and the other post-admission). The two cases of ventricular fibrillation took place in control group and both were defibrillated in exam room, evolving without sequelas and, afterwards, they were submitted to myocardial revascularization, as they showed multiple coronary severe lesions.

The series of octogenarians presented is modest and composes a retrospective study. As most patients were referenced by several physicians and institutions, information obtained is limited concerning hemodynamic studies and procedures that may have been subsequently performed, which prevented from a proper accuracy assessment of DASE in octogenarian patients, although such assessment was not the objective of this work.

Despite the lower use of atropine to complete DASE, octogenarian individuals achieved more maximum heart rate. There was a greater correlation between positive DASE for myocardial ischemia and absence of chest pain. Patients showed more rhythm disturbances, but general resolution was spontaneous. In our study, DASE showed to be a safe and feasible method for octogenarians.

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