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The declining frequency of inducible myocardial ischemia during stress echocardiography over 27 consecutive years (1983–2009)☆

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ABSTRACT

Background: Previous studies have suggested a decline in positivity of stress cardiac imaging, suggesting the need for developing better strategies for test selection to achieve acceptable cost-effectiveness balance. The aim of this retrospective study was to assess the rate of positivity of stress echocardiography (SE) over 27 consecutive years.
Methods: We assessed the rate of SE positivity in 2007 patients without previous myocardial infarction or coronary revascularization who performed SE in a tertiary care referral center from 1983 to 2009. SE was performed with dipyridamole (1427), dobutamine (136) or exercise (444).
Results: There was a progressive decline over time in the rate of SE positivity from 42% (1983–1991) to 22% (2001–2009), with a relative increase of patients with low pre-test probability of disease (from 5% to 27%). The percentage of patients studied with SE under anti-ischemic therapy increased markedly (from 8% in the first to 61% in the last nine years).
Conclusion: Over 27 consecutive years, we observed a steady decline in SE positivity rate (with >5-fold increase of low probability patients), with almost 8-fold increase in anti-ischemic therapy at testing. We probably need refined criteria of referral for testing and/or better ways to titrate the negative response beyond wall motion abnormalities during SE.

1. Introduction

Stress testing and, in particular, stress echocardiography (SE) are a valuable help for a modern practice of cardiology, and provide essential information for diagnosis and risk stratification in patients with known or suspected coronary artery disease (CAD) [1,2]. Their value is also witnessed by the increasing clinical use and incorporation in practice guidelines [3,4]. Yet, in recent years cardiovascular imaging has become the focus of intensive efforts on the part of public and private payers, since it has contributed substantially to the escalating health care costs in the last 20 years [5]. According to recent estimates, 20 to 50% of all SE examinations are partially or completely inappropriate [6–11], i.e., risks and costs may outweigh benefits [12]. Although SE is less expensive and risky than other alternative techniques and is radiation-free, nevertheless SE also contributes to imaging wastes and unwanted collateral damage, including the risks of the procedure itself with physical or pharmacological stressors [13–16] and the downstream impact of poor performance such as delay in diagnosis (false-negative results) or inappropriate diagnosis (false-positive results).

Recently, an impressive decline in rate of positivity has been reported for US outpatients studied with myocardial perfusion imaging from 1991 and 2009 [17], suggesting that we should change our referral patterns to be really cost-effective - provided that the observed results are true worldwide and also with different stress imaging techniques [18]. A similar finding was reported for exercise SE in Europe from 1997 to 2012 in a Spanish hospital setting [19].

Aim of this study was to assess the rate of positivity during cardiac stress testing by SE over 27 years in an unselected cohort of consecutive in-hospital patients. The study hypothesis is that cardiac stress testing positivity is declining over the years due to the assessment of lower CAD risk samples.

2. Methods

2.1. Study population

The study included 2007 patients consecutively hospitalized at the Institute of Clinical Physiology, National Research Council of Italy (CNR), Pisa, Italy, over 27 years (1983–2009) who underwent SE as screening test for CAD. At discharge, all demographic, history, clinical and instrumental data were collected in the Institute's dedicated cardiovascular database. For this study, data on risk factors, type of symptoms, diagnosis, and SE results were considered. Patients were excluded if they met one of the following criteria: age < 30 and >90 years, acute coronary syndrome, history of myocardial infarction, previous coronary revascularization (percutaneous coronary intervention or coronary artery bypass graft surgery). The exclusion criteria were applied for data analysis, not for stress testing.

The original Diamond–Forrester model was taken to calculate pretest CAD probability [20] which was classified as low (15%), intermediate (15–65%), and high (>65%).

☆ The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Exercise stress echo was conducted using a semi-supine bicycle ergometer with 25 W incremental loading every 2 min. Dipyridamole (up to 0.84 mg/kg over 10 min with co-administration of atropine up to 1 mg, or up to 0.84 mg/kg mg over 6 min) and dobutamine (up to 40 mcg/kg/min with co-administration of atropine up to 1 mg) stress echo were performed according to the well-established protocols [14].

The study was approved by the Pisa Ethical Committee on November 11, 2014 (Study Protocol n. 335/2014).

2.2. Statistical analysis

Continuous variables were reported as mean ± standard deviation. Categorical variables were expressed as percentages. Chi-square test with Yates correction was used to compare categorical data. The unpaired 2-tailed Student's *t*-test (continuous data) was used for continuous variables to compare groups. Whenever appropriate, Bonferroni correction was used for subgroup analysis.

The statistical significance of changes over time in different patients was assessed by the Cochran-Armitage test (for binary variables). Logistic regression analysis was performed to evaluate the risk-adjusted odds ratio of clinical factors predicting abnormal SE results. A two-sided P-values <0.05 was considered significant. Statistical analysis was performed using software R version 2.15.3.

3. Results

3.1. Temporal change in clinical profile of SE patients

The clinical characteristics of our patient population are shown in Table 1.

From the first (1983–1991) to the last (2001–2009) period of the study, there was a progressive increase in the mean age of our patient population (55 ± 9 vs 65 ± 12 years, P < 0.001), a mild increase in the percentage of women studied (from 30% to 37%, P = 0.016), a significant decline in the mean pre-test probability of CAD based on the type of referred symptom (with a decline in the percentage of typical angina referred for testing, P < 0.001). Overall, the patients showed a progressive decrease of mean pre-test likelihood of CAD. The % of patients with low pre-test probability (<15% on clinical grounds) significantly increased from 5% in the first period to 27% in the last one, with a significantly decrease of patients with high pre-test probability (from 70 to 47%) (Fig. 1).

Regarding risk factors, there was a decrease in the percentage of patients who were current smokers, but an increase in the percentage who had hypertension, high cholesterol, diabetes, and obesity. The percentage of patients with family history of CAD was stable over the years (Table 1).

There was a progressive increase in the use of lipid-lowering, antihypertensive medications and beta-blockers, and a decline in the use of nitrates and Calcium channel blockers (Table 1).

A pharmacological stress was performed in 1563 patients (dipyridamole in 1427, dobutamine in 136) and exercise SE in 444. The % of patients studied with dipyridamole significantly decreased from 100% in the first period to 83% in the second and 43% in the last one, with a significant increase of patients with exercise (from 0 to 6

Table 1
Clinical characteristics of population of 2007 patients.

Time period	1983–1991		1992–2000		2001–2009		P for trend
Patients, N - %	499–25		709–35		799–40		<0.001
Age (mean ± SD)	55 ± 9		62 ± 10		65 ± 12		<0.001
Male Sex N-%	347–70		450–63		503–63		0.016
Chest pain symptom	*N*	*%*	*N*	*%*	*N*	*%*	
Typical	351	70	448	63	324	41	<0.001
Atypical	129	26	132	19	179	22	<0.001
Non anginal pain	0	0	42	6	107	13	<0.001
Asymptomatic	19	4	87	12	189	24	<0.001
Diamond-Forrester score	73 ± 26		68 ± 32		54 ± 34		<0.001
Risk factors	*N*	*%*	*N*	*%*	*N*	*%*	
Family history	234	47	333	47	353	47	0.49
Diabetes	49	10	111	16	181	23	<0.001
Hypertension	154	31	347	49	552	69	<0.001
Hypercholesterolemia	85	17	349	49	457	57	<0.001
Hypertriglyceridemia	120	24	167	24	154	19	0.05
Smoking	284	57	292	41	337	42	<0.001
	N (%)	*mean ± SD*	*N (%)*	*mean ± SD*	*N (%)*	*mean ± SD*	
Body Mass Index	385 (77)	27 ± 3	536 (76)	27 ± 4	765 (96)	27 ± 4	
Normal	125 (33)	23 ± 2	163 (30)	23 ± 2	234 (31)	23 ± 2	0.77
Overweight	216 (56)	27 ± 1	265 (49)	27 ± 1	345 (45)	27 ± 1	0.002
Obese	44 (11)	32 ± 2	108 (20)	34 ± 4	186 (24)	33 ± 3	<0.001
Heart rate b/min	435	64 ± 7	571	71 ± 15	796	70 ± 16	<0.001
SBP N-mmHg	435	130 ± 15	571	133 ± 19	796	141 ± 22	<0.001
DBP N-mmHg		81 ± 8		77 ± 10		77 ± 11	<0.001
SE test	*N*	*%*	*N*	*%*	*N*	*%*	
SE positive, N 569, 28%	209	42	182	26	178	22	<0.001
Pharmacological positive	209	42	182	26	52	7	<0.001
Anti-ischemic therapy N 872, 77%	67	8	271	31	534	61	<0.001
Medications	N	%	N	%	N	%	
Statins			78	11	336	42	/
Betablockers	47	9	124	16	329	41	<0.001
ACE inhibitors			93	13	283	35	/
Nitrates	260	52	340	48	258	32	<0.001
Calcium channel blockers	344	69	320	45	122	15	<0.001
Anti-platelet agents	246	49	486	69	477	60	<0.001

SBP = systolic blood pressure; DBP = diastolic blood pressure; CAD = coronary artery disease; SE = stress echocardiography; ACE = angiotensin converting enzyme.