

Different Clinical Profile of Patients Undergoing Coronary Arteriography after Stress SPECT or Stress Echocardiography

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Abstract

Purpose: Stress SPECT and stress echocardiography show similar diagnostic accuracy in patients with known or suspected coronary artery disease. The choice of which imaging modality is the most suitable may depend on several factors, including local facilities and expertise, cost containment, biological risk related to the use of radiations, and the feasibility of stress echocardiography. We hypothesized that some of the above factors could shape the characteristics of patients undergoing one or the other imaging modality. Thus, we sought to investigate whether patients referred to coronary arteriography after stress SPECT or stress echocardiography differ in terms of clinical and risk profile.

Methods: We retrospectively analysed 1712 patients who had undergone stress SPECT (821 patients, 48%) or stress echocardiography (891 patients, 52%), followed by coronary arteriography (median, three days).

Results: Patients studied by stress SPECT did not differ from stress echo patients as to age and extent of coronary stenoses, but were less frequently female ($P=0.0021$), more frequently had severe obesity ($P=0.0102$), a previous myocardial infarction ($P=0.0009$), or severe left ventricular dysfunction ($P<0.0001$). During follow-up (median, 7 years), stress SPECT patients had a worst survival rate free from cardiac death and non-fatal infarction (81.4%) than stress-echo patients (85.6%, $P=0.015$).

Conclusion: In our centre, stress SPECT is more commonly performed in higher risk patients than stress echocardiography.

Keywords: Myocardial perfusion imaging; Stress echocardiography; Coronary artery disease; Stable angina; Prognosis

Introduction

According to European and American guidelines, stress SPECT and stress echocardiography show similar accuracy rates in the diagnostic work-up of patients with known or suspected coronary artery disease [1,2].

Stress echocardiography provides a few advantages over perfusion scintigraphy including higher specificity, greater versatility, better convenience (i.e. lower costs), and the use of non-ionizing radiations. Nonetheless, stress perfusion imaging assures higher technical success rates, higher sensitivity, and a better accuracy when multiple resting Left Ventricular (LV) wall motion abnormalities are present. As a result, the choice of which imaging modality is the most suitable may depend on several factors, including local facilities and expertise, cost containment, biological risk related to the use of radiations, and the feasibility of stress echocardiography in patients with a suboptimal acoustic window [3-5].

We hypothesized that some of the above factors could shape the characteristics of patients undergoing one or the other imaging modality. More specifically, the present retrospective study aims at ascertaining whether patients who have undergone stress SPECT or stress echocardiography, followed by invasive coronary arteriography, differ in terms of clinical presentation and risk profile.

Materials and Methods

Patients

The study included a retrospective cohort of consecutive patients, admitted to our Institute for known or suspected coronary artery

disease, who had undergone either stress/rest myocardial perfusion imaging by gated SPECT or stress echocardiography followed within one month by invasive coronary arteriography. The indications to stress imaging included the detection of myocardial ischemia in symptomatic or asymptomatic patients, and/or the detection of myocardial viability. Patients with acute coronary syndrome were excluded from the study, as well as patients with more than moderate valvular heart disease or known cardiomyopathy.

A study population of 1712 patients was selected spanning from 1996 till 2009. Each decision to risk-stratify patients by either stress perfusion scintigraphy or stress echocardiography was taken by the referring physician. The local committee on human research approved the study protocol. In addition, patients gave a written informed consent to have their clinical data prospectively collected for research purposes.

Clinical examination

The analysis was based on the following variables, collected for

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each patient: age, sex, cardiovascular risk factors, history of angina (at rest, on effort, or mixed), previous myocardial infarction, previous coronary artery bypass graft surgery, previous percutaneous coronary interventions, and LV ejection fraction (measured by two-dimensional echocardiography using single-plane or biplane Simpson's rule or by gated SPECT).

Stress SPECT

Gated SPECT was performed with a double head γ -camera (E. Cam; Siemens Medical Solutions, and Millennium MC; GE Healthcare) equipped with a high-resolution collimator. A standardized protocol, consisting of a 64 \times 64 matrix, 32 projections per head, 40-s projections, and eight frames per cycle, was applied with appropriate energy photopeaks [6]. Each patient underwent stress/rest gated SPECT according to a single-day protocol, choosing between bicycle exercise stress tests, dipyridamole stress tests (0.56 mg/kg I.V. over 4 min) or dobutamine stress test (up to 40 mg/kg/min). Standard protocols for the injection of ^{99m}Tc-tetrofosmin were used both during stress and at rest. Images were acquired from 15 to 45 min after stress and from 30 to 45 min after rest injections. All patients with previous myocardial infarction were subjected to baseline tracer injection after sublingual nitrates. In every patient, Quantitative Gated SPECT and Quantitative Perfusion SPECT programs were used both at rest and after stress according to a 17-segment model to obtain summed stress scores, summed rest scores and summed difference scores [7]. A study was considered positive for ischemia if the summed stress score was ≥ 4 according to previous studies on the prognostic impact of myocardial perfusion abnormalities [6]. SPECT interpretation always preceded coronary arteriography.

Stress echocardiography

Transthoracic stress echocardiography was performed with commercially available ultrasound scanners (Sonos 7500 or iE 33, Philips Ultrasound, Andover, Massachusetts; Sequoia C256 Acuson Siemens, Mountain View, California; Vivid System 7, GE/Vingmed, Milwaukee, Wisconsin) equipped with multifrequency phased-array sector scan probes and with second harmonic technology. Two-dimensional echocardiography and 12-lead electrocardiographic monitoring were performed in combination with bicycle exercise, high-dose dipyridamole (up to 0.84 mg I.V. over 6 min) or dobutamine (up to 40 mg/kg/min), according to standardized protocols [3]. Echocardiographic images were semiquantitatively assessed using a 17-segment, 4-point scale model of the LV [7]. The test was considered positive for ischemia if at least two adjacent segments worsen their function during stress. The interpretation of stress echocardiography always preceded coronary arteriography.

Coronary arteriography

Angiographic images were obtained from a femoral or a radical approach according to standard techniques, and were qualitatively analyzed for clinical purposes. A luminal diameter reduction $>50\%$ was considered a significant stenosis. The analyzed vessels included main coronary arteries (i.e. left main stem, left anterior descending, left circumflex, and right coronary arteries) and secondary branches (i.e. first diagonal, obtuse marginal branch or posterior descending artery). In case a vessel presented more than one stenosis, only the most severe one was considered.

Follow-up

Patients were followed-up with periodic examinations in the

outpatient setting. For those who did not attend this program, follow-up data were obtained by means of written telephone interviews (administered to the patient or the patient's family by ad hoc personnel) or mail questionnaires. In case of no replay, the local demographic registry was queried. Cardiac death was defined as death caused by acute myocardial infarction, heart failure, or a sudden and unexpected death not related to any possible cause; non-fatal infarction was documented by clinical records.

Statistical analysis

Continuous variables were expressed as mean \pm 1 SD or as median and interquartile range, and categorical variables as percentages. The difference in clinical and angiographic variables between the two groups of patients studied by stress SPECT or stress echocardiography was tested by the Analysis of Variance (ANOVA) for continuous variables, and by the chi-square test or the Fisher's exact test for qualitative variables. Survival curves were estimated by Kaplan-Meier method. The variation in the survival rate free from cardiac events (i.e. cardiac death and non-fatal infarction) between the two groups of patients was tested by Log-Rank test. All statistical tests were two-tailed; a $p < 0.05$ was considered significant. Statistical analysis was performed with commercially available software (JMP 9, SAS Institute Inc., Cary, North Carolina, USA).

Results

Stress imaging modalities

Out of 1712 patients with ascertained or suspected CAD, 821 (48%) underwent stress/rest SPECT and 891 (52%) stress echocardiography, followed by invasive coronary angiography within a median of three days [1-19 days]. Stress SPECT was obtained after bicycle exercise test in 586 patients (71%), after dipyridamole infusion in 228 (28%) and after dobutamine infusion in 7 patients (1%). Stress echocardiography was recorded after bicycle exercise in 425 patients (48%), after dipyridamole infusion in 407 (46%), and after dobutamine infusion in 59 patients (6%).

The choice of stress test was performed after clinical evaluation accordingly to absence of major contraindication in order to obtain the best expected sensitivity and specificity in detecting CAD. Pharmacological therapy with beta blockers were discontinued 72 hours before stress testing in all patients submitted to exercise stress test. No differences in terms of presence of left bundle branch block or arrhythmias were found in the two groups of patients submitted to stress SPECT or echocardiography.

Patients' clinical profile

Patients differed by several clinical variables, depending on the used imaging modality (Table 1). Those examined by stress SPECT were more frequently anginal-free than the ones undergoing stress echocardiography. Furthermore, patients examined by myocardial perfusion imaging showed a worst clinical profile than those examined by stress echocardiography, being less frequently female, more often severely obese, with a higher occurrence of previous myocardial infarction and showing more often severe LV dysfunction (ejection fraction $<35\%$). In 1332 cases, serum creatinine levels were also available: again, patients examined by SPECT showed elevated levels of creatinine (>1.4 mg/dl) more frequently (80 patients, 11%), than those studied by echocardiography (45 patients, 7%, $P=0.0219$). Vice versa the two groups did not differ as to the extent of coronary stenosis.

Variable	Stress SPECT (n = 821)	Stress Echocardiography (n = 891)	P
Age (y)	64.4 ± 10.0	63.8 ± 10.0	0.2279
Male	662 (81%)	663 (74%)	0.0021
Female	159 (19%)	228 (26%)	
Angina on effort	212 (26%)	203 (23%)	0.027
Angina at rest	149 (18%)	157 (18%)	
Mixed angina	225 (27%)	317 (35%)	
Angina-free	235 (29%)	214 (24%)	
Previous myocardial infarction	346 (42%)	306 (34%)	0.0009
Previous CABG surgery	67 (8%)	85 (10%)	0.3162
Previous PCI	142 (17%)	160 (18%)	0.7198
Family history of CAD	410 (50%)	421 (47%)	0.2661
Diabetes mellitus	187 (23%)	207 (23%)	0.8231
Arterial hypertension	489 (49%)	519 (51%)	0.8715
Hypercholesterolemia	549 (67%)	600 (67%)	0.8360
Obesity (BMI 30-34.9 kg/m ²)	169 (22%)	162 (20%)	0.3619
Severe obesity (BMI ≥ 35 kg/m ²)	43 (6%)	24 (3%)	0.0102
Smoker within last year	382 (47%)	434 (49%)	0.4478
LVEF 35-45%	99 (12%)	87 (10%)	0.1538
LVEF <35%	132 (16%)	67 (8%)	<0.0001
Single-vessel CAD	222 (27%)	230 (26%)	0.5505
Double-vessel CAD	163 (20%)	166 (19%)	
Triple-vessel CAD	107 (13%)	110 (12%)	
Left main stenosis	48 (6%)	71 (8%)	
Stenosis in secondary branches	41 (5%)	47 (5%)	
No significant stenoses	240 (29%)	267 (30%)	

Data are numbers of patients, with percentages in parentheses, or mean ± SD.

CABG: Coronary Artery Bypass Graft; PCI: Percutaneous Coronary Interventions; CAD: Coronary Artery Disease; BMI: Body Mass Index; LVEF: Left Ventricular Ejection Fraction

Table 1: Clinical and Angiographic Characteristics of Patients (n=1712)

Follow-up

During follow-up (median, seven years), 201 patients developed cardiac events, namely cardiac death in 134 cases, and non-fatal myocardial infarction in 67 cases. As shown in Figure 1, patients studied by stress SPECT had a worse cardiac event-free survival rate at 10 years (81.4 ± 1.7%) compared to those studied by stress echo (85.6% ± 1.5, P=0.0155 by Log -Rank).

Discussion

Based on the results of this study patients undergoing stress SPECT or stress echocardiography, followed by coronary arteriography, present different clinical profiles.

Considering the higher biological risk of using radiations in younger patients, an older age could be expected in patients examined by myocardial perfusion imaging than by echocardiography. This was not the case in our patients with ascertained or suspected ischemic heart disease, likely because very few of them were young, the median age being 64 years and the inter quartile range 57-71 years. Concerns about

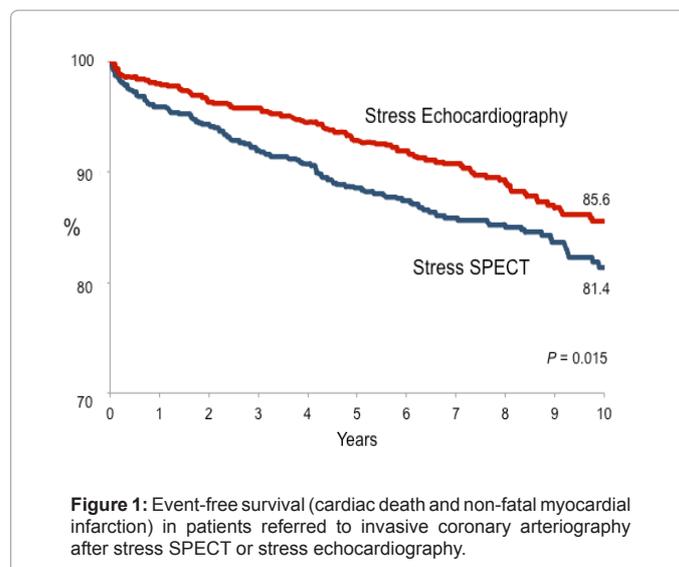


Figure 1: Event-free survival (cardiac death and non-fatal myocardial infarction) in patients referred to invasive coronary arteriography after stress SPECT or stress echocardiography.

the risk of ionizing radiations in female subjects likely contributed to the lower prevalence of women among patients studied by stress SPECT.

The higher occurrence of severe obesity in patients studied by stress SPECT, compared to those studied by stress echocardiography, reflects probably the technical difficulties of ultrasound imaging in these subjects. Unfortunately, our data base does not include an additional variable that is often associated to inadequate acoustic window that is chronic obstructive pulmonary disease.

Less obvious is the higher incidence of previous myocardial infarction and severe LV dysfunction in patients studied by means of stress SPECT, than by stress echocardiography. The choice of myocardial perfusion imaging in these subjects might be related to the limited ability of echocardiography in detecting new wall motion abnormalities in patients with extensive LV dysfunction, and/or to a preference of local referring physicians. Similar considerations could also apply to the higher prevalence of anginal-free patients among the subjects studied by stress SPECT. As a matter of fact, 23% of our patients who did not refer anginal symptoms had a LVEF <35%, while only 8% of anginal patients had a LVEF <35%. Thus, the higher prevalence of asymptomatic patients referred to stress SPECT likely reflects a greater confidence of referring physicians on myocardial perfusion for the assessment of myocardial viability and ischemia in patients with severe LV dysfunction.

Ultimately, from the above listed patient characteristics we can derive a higher risk profile of patients undergoing stress SPECT, as variations of event-free survival rates show in real settings.

Study Limitations

Being based on a retrospective analysis, limited to one Institute, the present study is unavoidably influenced by some limiting factors. Furthermore, data were extracted from a clinical data base of patients who had all undergone coronary arteriography. Thus, the reached conclusions cannot be extended to patients referred to stress imaging, but in whom coronary arteriography was not highlighted.

Our nuclear cardiology and echocardiography laboratories have been functioning for several years, as demonstrated by the similar number of patients undergoing one of the two modalities, before

invasive coronary arteriography, in a time frame of thirteen years. Thus, the feasibility issue of the two tests could not be explored.

Finally, we have not examined the appropriateness of stress imaging, which is able to affect both diagnostic accuracy and prognostic stratification [8].

Conclusion

In our centre, stress SPECT is more commonly performed in higher risk patients than stress echocardiography.

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