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International Journal of Cardiology 98 (2005) 191–197

International Journal of Cardiology

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Review

# Diagnostic value of stress echocardiography for the detection of restenosis after PTCA

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Received 25 October 2003; received in revised form 3 February 2004; accepted 29 February 2004
Available online 14 July 2004

**Abstract**

Stress echocardiography (SE) has become a widely accepted clinical tool for the non-invasive diagnosis of coronary artery disease (CAD). Previous studies have confirmed that SE has superior diagnostic value compared to exercise ECG testing. SE has also emerged as a cost-effective alternative to nuclear imaging techniques in patients where symptoms and/or conventional ECG stress testing have provided ambiguous results. Several studies have investigated the value of SE to detect significant restenosis after PTCA. However, in these studies, different methods have been used to induce cardiovascular stress such as physical exercise by bicycle or treadmill, pharmacologic stress testing (with dipyridamole or dobutamine) or transoesphageal atrial pacing. This review evaluates the published database of SE to detect restenosis in patients after successful PTCA. It includes 13 studies with a total of 989 patients performed at 3–6 months after the primary intervention. The diagnostic value, utility and limitations of SE is presented and discussed. The data show that SE has a high diagnostic value for detecting significant restenosis after PTCA. Mean sensitivity of SE was 74% (CI 69–79%), mean specificity was 87% (CI 84–89%). The positive predictive value (PPV) of SE was 83%, the overall negative predictive value (NPV) 97%. We conclude that, in the follow-up of patients after PTCA, SE has distinct advantages over other non-invasive methods and is a recommended method for the detection of those to be considered for repeat angiography.


*Keywords:* Stress echocardiography; Dipyridamole echocardiography; Exercise echocardiography; Dobutamine echocardiography; Restenosis; PTCA; Angioplasty

## 1. Introduction

### 1.1. The problem of non-invasive detection of restenosis

The era of coronary stenting has definitively reduced the restenosis rate after successful PTCA and now the majority of patients in many countries receive primary coronary stenting. However, the problem of restenosis after PTCA has not disappeared and the difficulty of diagnosing suspected restenosis has not been resolved satisfactorily. Despite the widespread use of stents, restenosis still occurs in approximately 20–30% of patients who have undergone successful PTCA [1–3]. Outside the setting of controlled clinical trials, routine angiographic follow-up at 3–6 months cannot be routinely recommended. Besides the lack of prospective evidence to support this procedure there is limited capacity of catheterisation laboratories and the inherent costs of repeat angiography in all patients undergoing PTCA are high. Interestingly, it has never been documented in large prospective studies that patients with a significant restenosis actually benefit from a second intervention. However, it seems intuitive to treat a recurrent restenosis on the same rationale as the initial intervention, assuming that the original indication was based on current guidelines for coronary interventions. This issue is even more complex as recurrence of symptoms like angina and shortness of breath during daily activities or exercise have are relatively poor predictors of restenosis [4–6]. In addition, the low sensitivity and specificity of recurrent symptoms or ST-abnormalities during bicycle- or treadmill exercise testing has been clearly demonstrated in several studies [7–11]. This is further complicated by the well-described problem of asymptomatic restenosis in a considerable number of patients with risk factors for restenosis such as diabetes [4,6,11]. Therefore, physicians managing

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doi:10.1016/j.ijcard.2004.02.012

post-PTCA patients are confronted with the diagnostic dilema of how to select the 'right patients', namely those with a high probability of showing "significant" restenosis, appropriate for intervention.

In an attempt to resolve this important issue, several studies have combined physical or pharmacological stress testing with nuclear imaging techniques like thallium scintigraphy or positron emission tomography (PET) [5,12–15]. Nuclear imaging could indeed increase the sensitivity and specificity for the detection of patients with significant restenosis, however, nuclear imaging is comparatively expensive and not widely available. Thus, the non-invasive detection of patients with restenosis after successful PTCA remains an unsolved diagnostic problem.

The diagnostic value of stress echocardiography (SE) for the detection of patients with significant restenosis after PTCA has been investigated by several authors using different protocols to induce cardiovascular stress: physical exercise by treadmill testing or bicycle [1–20] or pharmacological stress by the infusion of dipyridamole [4,11,21] or dobutamine [22–24] and transesophageal atrial pacing [25,26].

The primary objective of this review is to evaluate the current evidence base on SE performed at 3–6 months after successful PTCA with regard to diagnostic value, utility and limitations to detect significant restenosis.

## 2. Methodology

We conducted a MEDLINE search using the key terms "stress echocardiography", "exercise echocardiography", "dipyridamole echocardiography", "dobutamine echocardiography" either alone and/or in combination with the key term "restenosis", "PTCA" and "angiography" for the years 1989–2003. Since in most patients significant restenoses occurs within 3–6 months after the intervention, only studies covering this time interval were reviewed. All publications were screened by two of the authors (AS, SP) to determine if they met the primary objectives of this review: (1) the SE test was performed 3–6 months after successful PTCA, (2) the SE test was performed before repeat angiography and was interpreted blinded to the angiographic results, (3) the outcome of the SE test did not influence the decision for repeat angiography and (4) interpretation of the angiogram was independent and blinded to the SE test result. In addition to the MEDLINE search, any papers or published abstracts that were cross-referenced in the respective publications and met the above criteria for the this review were included. The results for sensitivity and specificity as reported in the original manuscripts/abstracts are given in Table 1. The confidence intervals were calculated using the exact method [27]. The positive (PPV) and negative predictive values (NPP) were calculated using the respective standard formula.

## 3. Stress echocardiography for the detection of restenosis

We describe the methodology, results and limitations of the included studies/methodology categorised by Exercise Echocardiography, Pharmacological Stress Echocardiography and Transoesophageal Pacing.

### 3.1. Studies using exercise echocardiography

In total we found 523 patients investigated in SE studies using physical exercise by either treadmill- ($n=357$) or bicycle-testing ($n=166$). Sensitivity from 67% to 87% and specificity from 83% to 95% were reported [16–20] (Table 1). In only one of these five studies [18], beta blocker

Table 1
Studies investigating the diagnostic value of stress echocardiography (SE) 3–6 months after successful PTCA

| Author | Methodology | Patients | Sensitivity | Specificity | Resten. def. | Angiographic assessment |
|---|---|---|---|---|---|---|
| Bengston [16] | Treadmill | 71 | 71% | 87% | >60% | quantitative |
| Kramer [17] | Treadmill | 185 | 82% | 95% | not reported | not reported |
| Aboul-Enein [18] | Treadmill | 101 | 67% | 83% | >50% | visual |
| Mertes [19] | Bicycle | 86 | 83% | 85% | >50% | visual |
| Hecht [20] | Bicycle | 80 | 87% | 95% | >50% | quantitative |
| Pirelli [4] | Dipyridamole | 75 | 71% | 90% | >70% | quantitative |
| Pirelli [11] | Dipyridamole | 50 | 75% | 90% | >70% | quantitative |
| Scherhag [21] | Dipyridamole | 65 | 74% | 98% | >70% | quantitative |
| Takeuchi [22] | Dobutamin | 53 | 78% | 93% | >50% | visual |
| Heinle [23] | Dobutamine | 103 | 38% | 79% | >50% | quantitative |
| Schnaak [24] | Dobutamine | 50 | 67% | 93% | >50% | quantitative |
| Hoffmann [25] | atrial pacing | 50 | 72% | 50% | >70% | not reported |
| Stemple [26] | atrial pacing | 20 | 85% | 86% | >75% | not reported |
| **Summary** | | **989** | **74% (CI 69–79%)** | **87% (CI 84–89%)** | | |

Resten. Def.: Definition of the percentage lumen narrowing rated assignificant restenosis.
Angiographic Assessment: Methodology of angiographic assessments. Quantitative: measurement of coronary lumen narrowing done by quantitative angiography. Visual: measurement of coronary lumen narrowing done by two experienced investigators blinded to the echocardiographic results.