Long-term prognosis of normal stress-only gated myocardial perfusion imaging in 1,000 patients over a 5-year follow-up period

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Abstract

Objective: Gated myocardial perfusion imaging (GMPI) is a cornerstone non-invasive tool for diagnosing and risk stratifying patients with suspected or known coronary artery disease (CAD). Stress-only protocols are advocated in guidelines due to reduced radiation exposure and cost, but long-term data on the absence of major adverse cardiac events (MACE) in a large cohort is valuable. This study aimed to evaluate the long-term outcomes in a large cohort of patients who underwent a normal stress-only myocardial perfusion imaging (MPI) and had no major adverse cardiac events over a 5-year follow-up period. **Subjects and Methods:** We retrospectively analyzed data from 1000 consecutive patients referred for MPI due to suspicion of stable CAD between 21/05/2018 and 21/7/2025. All patients underwent a stress-only MPI protocol. Only patients with visually interpreted normal stress scans were included in the analysis. The primary endpoint was the occurrence of major adverse cardiac events (MACE), defined as cardiac death or non-fatal myocardial infarction (MI), as ascertained through telephone interview and standardized follow-up over a median of 5 years. **Results:** The study population included 1000 patients (mean age: 65.4±10.7 years), (43.4% male). All patients had normal stress-only myocardial perfusion scans. During the median 5-year follow-up period, no major adverse cardiac events (cardiac death or MI) were recorded using telephone interviews across the entire cohort. The annualized cardiac event rate was 0%, reinforcing previously reported low event rates of less than 1% per year for normal studies. **Conclusion:** In this large cohort of patients presenting with symptoms of stable CAD who had normal findings on GMPI, the complete absence of major adverse cardiac events over a median 5-year follow-up period (only one experienced 1 vessel coronary artery disease 6 years post GMPI) confirms the robust negative predictive value of this imaging modality. These findings support the use of a normal stress-only protocol for identifying a low-risk patient population in whom further aggressive diagnostic workup may not be necessary.

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Introduction

Gated stress-only myocardial perfusion imaging (GMPI) is increasingly utilized in nuclear cardiology to minimize patient radiation exposure, shorten scan times, and improve laboratory efficiency. Traditional protocols typically involve both stress and rest imaging; however, if stress images appear normal, rest imaging may be omitted. Previous studies have demonstrated that a normal GMPI yields similarly favorable outcomes compared to conventional rest-stress protocols [1, 2].

Nevertheless, the widespread adoption of stress-first or stress-only protocols has been somewhat limited by concerns over long-term prognostic reliability, especially in large real-world cohorts. Clinical data from everyday practice-beyond highly controlled or small research populations-are needed to validate that patients with normal stress-only GMPI can safely avoid rest imaging without compromising prognostic safety.

To address this gap, we conducted a retrospective cohort study of 1,000 consecutive patients who underwent gated stress-only GMPI, had normal perfusion and left ventricular (LV) function, and no documented cardiac events during follow-up. Our primary objective was to assess the long-term incidence of major adverse cardiac events (MACE) in this population, thereby evaluating the prognostic value of a normal stress-only pro-tocol in a large "real-life" sample.

Subjects and Methods

Study design and population

We performed a retrospective cohort study including 1,000 consecutive patients who underwent stress-only single photon emission computed tomography (SPECT) MPI at Onassis Cardiac Surgery Center. The inclusion criteria were:

1. Normal stress perfusion imaging.
2. No history of myocardial infarction.
3. Adequate image quality, and
4. Completed follow-up data for cardiac events.

The exclusion criteria included abnormal stress perfusion, or incomplete imaging data.

Imaging protocol

Written informed consent was obtained from each patient to be submitted to the stress-only protocol and for the use of the data for scientific purposes. Gated stress MPI was performed with technetium-99m (^{99m}Tc) compounds (sestamibi or tetrofosmin) on a GE Millenium VG5/Discovery camera ^{99m}Tc-sestamibi or ^{99m}Tc-tetrofosmin was injected at the peak of the stressor (pharmacological or exercise stress test) and images were acquired according to the EANM Guidelines [3]. Attenuation correction was not used. In equivocal cases an additional prone study was acquired. The images were evaluated visually by two independent Nuclear Medicine physicians blindly.

Follow-up and end points

- Follow-up duration: 5.6 years mean
- Data collection: telephone interviews
- Primary endpoint: major adverse cardiac events (MACE), defined as cardiac death, hospitalization or non-fatal myocardial infarction
- Secondary endpoints: all-cause mortality, coronary revascularization (PCI or CABG)

Results

One thousand patients (mean age: 65.4±10.7 years) were studied with gated stress-only GMPI 5 years (median time) before, the referrals made by clinician cardiologists on clinical judgement. Concerning the type of test, four hundred and fourteen patients (41.4%%) underwent pharmacological stress test using adenosine, five (0.5%) patients underwent dobutamine stress test, five hundred and seventy (57.0%) patients underwent exercise stress test using Bruce protocol and eleven (1.1%) underwent modified Bruce protocol (Tables 2, 3). If stress scan proved normal, the rest scan was omitted after patients' informed consent. In this cohort, four hundred and thirty-four (43.4%) patients were men, five hundred and sixty-six (56.6%) were women, six hundred and forty-six (64.6%) being less than 70 years of age and three hundred and fifty-four (35.4%) over 70 years of age. Seven hundred and ninety-nine (79.9%) patients were diabetics, six hundred and thirty-nine (63.9%) patients had hyperten-sion, six hundred and thirty-five (63.5%) had dyslipidemia and three hundred and thirty-three (33.3%) positive family history for coronary artery disease CAD. Also, two hundred and forty-one (24.1%) were smokers. Most patients were asymptomatic (54.1%), two hundred and sixty (26.0%) had atypical chest pain, ninety-nine (9.9%) had dyspnea, forty (4.0%) had fatigue and sixty (6.0%) had palpitations (Table 1).

In our cohort of 1,000 patients during the median 5-year follow-up period, no major adverse cardiac events (cardiac death or MI) were recorded using telephone interviews across the entire cohort. Only one diabetic and hypertensive patient who had one vessel coronary artery disease experienced chest pain 6 years post gated stress-only GMPI The annualized MACE rate was 0%.

Table 1. *Demographic and clinical characteristics of the study sample.*

	N (%)
Gender	
Female	566 (56.6)
Male	434 (43.4)
Age	
<70	646 (64.6)
70+	354 (35.4)
Diabetes mellitus	
No	799 (79.9)
Yes	201 (20.1)
Arterial hypertension	
No	360 (36.0)
Yes	639 (63.9)
N/A	1 (0.1)
Dyslipidemia	
No	364 (36.4)
Yes	635 (63.5)
N/A	1 (0.1)
Family history of heart disease	
No	666 (66.6)
Yes	333 (33.3)
N/A	1 (0.1)

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Smoker	
Non smoker	622 (62.2)
Smoker	241 (24.1)
Ex smoker	136 (13.6)
N/A	1 (0.1)
Reasons for ordering test	
Check	976 (97.6)
Atypical chest pain	7 (0.7)
Arrhythmias	3 (0.3)
Previous MI	1 (0.1)
Dyspnoea	2 (0.2)
Previous ischaemia test positive	1 (0.1)
Atypical chest pain & Arrhythmias	1 (0.1)
Atypical chest pain & family hist.	1 (0.1)
N/A	8 (0.8)
Coronary angiography	
No angiography	787 (78.7)
No CAD or lum. occl. LM<50%, rest coron <70%	66 (6.6)
Occlusion LM>50%, rest coronary > 70%	147 (14.7)
Symptoms	
No symptoms	541 (54.1)
Atypical chest pain	260 (26.0)
Dyspnoea	99 (9.9)
Fatigue	40 (4.0)
Palpitation	60 (6.0)
LVEF (echocardiogram)	
No test	446 (44.6)
>=55%	499 (49.9)
<55%	55 (5.5)
Total	1000 (100.0)
	Mean (SD)
Age	65.4 (10.7)

N/A: not available, lum. occl. : luminal occlusion

In our cohort of 1,000 patients with normal gated stress-only GMPI no patient had a MACE over the median five year follow-up period; only one diabetic and hypertensive patient experienced chest pain 6 years post gated stress-only GMPI who had one vessel coronary artery disease.

Table 2. *Type of test and related characteristics.*

	N (%)
Test	
Adenosine	414 (41.4)
Bruce	570 (57.0)
Dobutamine	5 (0.5)
Modified Bruce	11 (1.1)
Dyspnoea during test	
No	971 (97.1)
Yes	26 (2.6)
N/A	3 (0.3)
Chest pain during test	
No	956 (95.6)
Yes	43 (4.3)
N/A	1 (0.1)
Heart arrhythmias during test	
No	866 (86.6)
Yes	133 (13.3)
N/A	1 (0.1)
Fatigue during test	
No	896 (89.6)
Yes	103 (10.3)
N/A	1 (0.1)

(Continued)

Headache during test	
No	906 (90.6)
Yes	94 (9.4)
Flushing during test	
No	982 (98.2)
Yes	18 (1.8)
ST changes during test	
No	780 (78.0)
Yes	220 (22.0)
Total	1000 (100.0)
	Mean (SD)
Duration (mins) of Bruce test	7.8 (2.2)
Systolic BP (baseline)	131.4 (17.8)
Diastolic BP (baseline)	76.7 (7.3)
Systolic BP (peak)	160.4 (33.2)
Diastolic BP (peak)	84.1 (10.9)
Heart rate (baseline)	76.0 (14.3)
Heart rate (peak)	119.3 (32.5)

Table 3. *Patient's other characteristics.*

	N (%)
Previous arrhythmias	
No	972 (97.2)
Yes	27 (2.7)
N/A	1 (0.1)
Pacemaker implantation	
No	989 (98.9)
Yes	9 (0.9)
N/A	2 (0.2)
Defibrillator	
No	1000 (100.0)
PTCA	
No	889 (88.9)
Yes	108 (10.8)
N/A	3 (0.3)
CAD	
No	838 (83.8)
Yes	123 (12.3)
N/A	39 (3.9)
CABG	
No	895 (89.5)
Yes	31 (3.1)
N/A	74 (7.4)
Total	1000 (100.0)
	Mean (SD)
Time gap (years)	9.4 (5.6)

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Discussion

A normal GMPI test indicates good blood flow to the heart muscle during stress and suggests a low risk of life-threatening CAD. If the stress images fulfill the criteria as being normal in terms of perfusion and left ventricular function, the patients are excluded from a rest imaging. Patients' follow-up is accomplished on clinical criteria. The stress-only protocol is a time and radiation saving alternative to the standard stress/rest test as it skips the rest imaging portion, if the stress images are normal.

Duvall et al. (2010) compared mortality rates, both overall and cardiac, in two cohorts consisting of low-risk patients for CAD who underwent stress-only (1,673 patients) and stress-rest (3,237 patients) GMPI, respectively. At the end of follow-up (40±9 months), the cardiac mortality was 0.4% in the stress-only group and 0.5% in the rest-stress group [1]. Normal results not only in terms of perfusion pattern, but also in terms of LV function typically have an excellent short-term prognosis and are considered to have a low risk of cardiac events [4].

Gutstein et al. (2018) compared the annual mortality rates of supine-prone stress-only GMPI (1.3%), supine stress-only (1.5%) and full stress-rest GMPI (1.5%), respectively. The authors concluded that scanning in the prone position increases the number of stress-only GMPIs performed [6].

Nappi et al. (2020) examined long-term prognosis in a cohort consisting of 2106 patients with known or suspected CAD who underwent low-dose stress-only GMPI with a wide beam iterative reconstruction algorithm. The follow-up period was 6.6±2.7 years and the annualized major cardiac event rate was 1.2%, increasing with age especially in the presence of diabetes [5].

Malamitsi et al. (2021) repeated stress-only GMPI after a mean period of 4.9 years in a group of 340 patients who initially had a normal stress-only study and 91.2% out of them had again a normal stress-only study. On multivariable analysis patients who had family history of CAD combined with diabetes mellitus and hypertension had a 10.7 times higher risk of an abnormal GMPI than the patients without. In terms of prognosis these results prove stress-only GMPI to be a reliable method for follow-up of low and intermediate pretest probability CAD patients [2].

Cadmium zinc telluride (CZT) SPECT cameras, machine learning guidance and prediction models have been used in the selection of patients for stress-only GMPI with increasing prognostic safety [7-9].

In our study in a cohort of 1000 patients presenting with symptoms of stable CAD who had normal findings on GMPI, no major adverse cardiac events were stated by the examined patients on telephone interviews over a median 5-year follow-up period, therefore the annualized major cardiac event rate was 0%. There was only one patient who experienced chest pain due to one vessel coronary artery disease 6 years post GMPI. These findings suggest that a normal stress-only protocol provides excellent prognostic value in a real-world clinical population without apparent short-term cardiac events, they confirm the robust negative predictive value of stress-only GMPI as an imaging modality and support the use of a normal stress-only protocol for identifying a lower-risk patient population for CAD in whom further aggressive diagnostic workup may not be needed.

Clinical implications

- **Radiation safety & efficiency:** The stress-only strategy can reduce cumulative radiation dose and shorten imaging times, which is highly beneficial for patient safety and departmental throughput.
- **Risk stratification:** For patients who present with low to intermediate pre-test likelihood of CAD and have normal stress-only MPI, clinicians can confidently defer rest imaging, reserving it for patients with equivocal stress images or other clinical concerns.
- **Cost-effectiveness:** By avoiding unnecessary rest scans, costs may be reduced, both in terms of tracer usage and scanner time. Previous work supports that stress MPI is a cost-effective risk stratification tool in patients without known CAD [6].

Limitations

- **Retrospective Design:** As with all retrospective studies, selection bias may be present.
- **Event Rate & Power:** If the MACE rate is very low, the power to detect predictors in a multivariable model may be limited.
- **Follow-Up Accuracy:** Some events might be missed if follow-up relies on medical records or patient self-report.
- **Generalizability:** Single-center data may not reflect experience in other institutions, especially those with different patient demographics or imaging protocols.

Future Directions

- A prospective multicenter registry of stress-only GMPI could validate our findings across different populations and imaging systems.
- Investigate whether advanced imaging tools (e.g., CZT cameras, AI-based reconstruction) further improve the safety and efficiency of stress-only protocols.
- Evaluate patient subgroups (e.g., diabetics, elderly) more deeply to identify which populations most benefit from stress-only imaging.

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