ORIGINAL ARTICLE

Ischemia burden on stress SPECT MPI predicts long-term outcomes after revascularization in stable coronary artery disease

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Background. It is not entirely clear whether ischemia burden on stress single-photon emission computed tomography (SPECT) effectively identifies patients who have a long-term benefit from coronary revascularization.

Methods. The study population consisted of 719 patients with ischemia on stress SPECT. Early coronary revascularization was defined as percutaneous coronary intervention or coronary artery bypass grafting ≤90 days after SPECT. Patients who underwent late revascularization (>90 days after SPECT) were excluded (*n* = 164).

Results. Of the 538 patients (73% men, mean age 59.8 ± 11 years), 348 patients had low ischemia burden (<3 ischemic segments) and 190 patients had moderate to high ischemia burden (≥3 ischemic segments). A total of 76 patients underwent early revascularization. During a median follow-up of 12 years (range 4-17), 283 patients died of whom 125 due to cardiac causes. Early revascularization was beneficial on all-cause mortality (HR 0.46, 95% CI 0.30-0.46) and cardiac mortality (HR 0.54, 95% CI 0.29-0.99).

Conclusions. Patients with myocardial ischemia on stress SPECT who underwent early revascularization had a lower all-cause mortality and cardiac mortality during long-term follow-up as compared to patients who received pharmacological therapy alone. This difference in long-term outcomes was mainly influenced by the survival benefit of early revascularization in the patients with moderate to high ischemia burden. (J Nucl Cardiol 2016)

Key Words: Early revascularization • long-term • ischemia • SPECT

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Abbreviations

CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
PCI	Percutaneous coronary intervention
ECG	Electrocardiography
MBq	Megabecquerel
MI	Myocardial infarction
MPI	Myocardial perfusion imaging
SPECT	Single-photon emission computed tomography
99mTc	Technetium-99m

INTRODUCTION

Advances in pharmacotherapy have substantially improved the symptoms and long-term outcomes of patients with stable coronary artery disease (CAD) over the last decades. A subset of these patients may also benefit from coronary revascularization. The survival benefit of coronary revascularization is related to the amount of myocardial ischemia. Stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is a reliable tool to assess the ischemia burden and may be used to identify coronary revascularization candidates.[1] Patients with CAD and ischemia on stress SPECT have higher risk of all-cause mortality and myocardial infarction (MI) compared to patients without ischemia.[2] Previous data showed that coronary revascularization may be beneficial over medical therapy in patients with moderate to severe ischemia.[3] Randomized trials showed that early revascularization showed no improvement in all-cause mortality or myocardial infarction (MI) compared to optimal medical therapy.[4,5] However, nuclear substudies of these randomized trials are conflicting.[6,7] Moreover, long-term information after early coronary revascularization in patients with ischemia on stress SPECT is lacking. Therefore, the primary aim of this study was to evaluate the impact of early coronary revascularization on long-term outcomes in patients with myocardial ischemia on stress SPECT. The second goal was whether the ischemia burden on stress SPECT determines the prognostic benefit of revascularization.

METHODS

Study Design

A total of 2215 consecutive patients who underwent stress SPECT between November 1990 and May 2002 (Figure 1) were screened. Patients who had no ischemia (ischemia was defined as the presence of a reversible or partially reversible perfusion defect) on stress SPECT were excluded. Of this study population, 75 patients were excluded because of uninterpretable or missing SPECT data. The initial study population consisted of 719 patients with ischemia. Follow-up was complete in 702 (98%) patients. Early coronary revascularization was defined as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) ≤90 days after SPECT MPI. Patients who underwent late revascularization (defined as >90 days after SPECT MPI) were also excluded ($n = 164$). Thus, the data presented are based on a final study population of 538 patients. Patients underwent exercise bicycle ($n = 220$) or dobutamine ($n = 318$) stress SPECT. At the time of this study, dobutamine was the preferred stressor in our nuclear cardiology laboratory. The type of stress test was selected based on the patient's ability to exercise. During the period in which the stress test was performed, both bare metal stents (from the middle of 1993, n = 71) and drug-eluting stents were implanted (from 2000, n = 5). Before the stress test, a structured clinical interview and cardiac risk factors were acquired. A blood pressure ≥140/90 mm Hg or treatment with antihypertensive medication was considered as hypertension. A fasting glucose level ≥7.8 mmol/L or the need for insulin or oral hypoglycemic agents was considered as diabetes mellitus. A total cholesterol ≥6.4 mmol/L or treatment with lipid-lowering medication was considered as hypercholesterolemia. Heart failure was defined according to the New York Heart Association classification.[8] All patients gave informed consent before testing and consented participation in this study. The local ethics committee approved the study protocol.

Stress Test Protocol

Symptom-limited, upright, bicycle ergometry with stepwise increments of 20 W every minute was performed. Three electrocardiographic leads were continuously monitored. Cuff blood pressure measurements and 12-lead electrocardiograms were recorded at rest and every minute during exercise and recovery. In patients who were unable to perform exercise tests, dobutamine stress testing was performed as previously reported.[9] Dobutamine was administered intravenously, starting at a dose of 5 µg/kg/minutes for 3 minutes, then 10 µg/kg/minutes for 3 minutes, increasing by 10 µg/kg/minutes every 3 minutes up to a maximum dose of 40 µg/kg/minutes. If the test endpoint was not reached at a dobutamine dose of 40 µg/kg/minutes, atropine (up to 2 mg) was given intravenously. Blood pressure, heart rate, and electrocardiography were monitored continuously. Test endpoints were achievement of target heart rate (85% of maximum age and gender-predicted heart rate), horizontal or downsloping ST-segment depression >2 mm at an interval of 80 ms after the J point, ST-segment elevation >1 mm in patients who had no previous myocardial infarction, severe angina, systolic blood pressure decrease >40 mm Hg, blood pressure >240/120 mm Hg, or significant cardiac arrhythmias.

SPECT Imaging

An intravenous dose of 370 MBq of ^{99m}Tc-tetrofosmin ($n = 234$) or ^{99m}Tc-sestamibi ($n = 304$) was injected

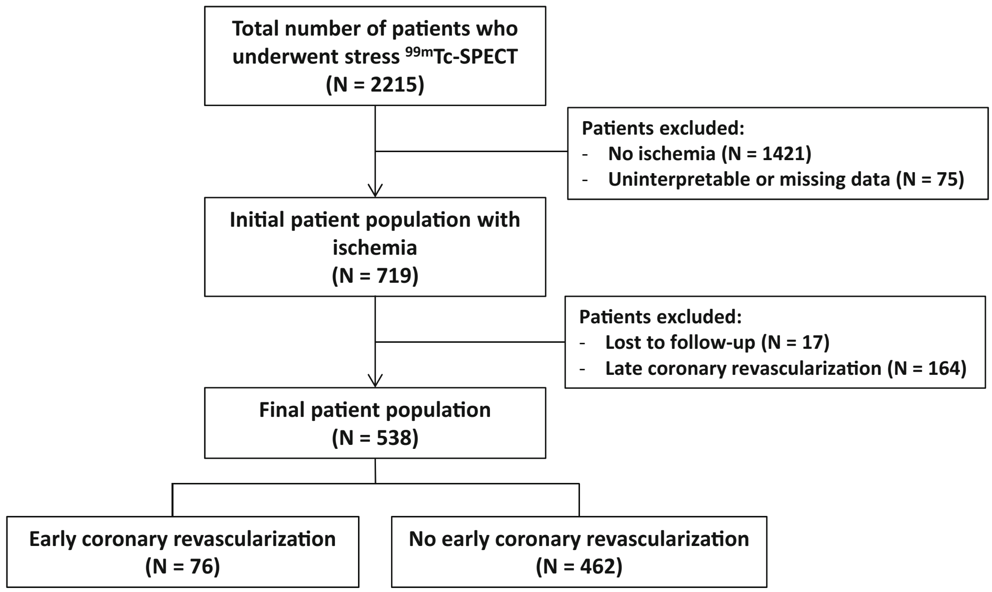

Figure 1. CONSORT diagram of the study population selection.

approximately 1 minute before the cessation of exercise. In rest studies, 370 MBq of tetrofosmin or sestamibi was administered at least 24 hours after the stress test. Myocardial images were acquired with a triple-head gamma-camera system (Picker Prism 3000 XP, Cleveland, Ohio, USA). Data were stored in a 64×64 matrix. The image data were reconstructed by filtered backprojection using a Butterworth filter (cutoff frequency, 0.17 cycles per pixel); 6-mm-thick (1 pixel) transaxial slices were obtained. The interpretation of the SPECT was semi-quantitatively performed by visual analysis and aided by circumferential profiles analysis. Stress and rest tomographic views were reviewed side by side by an experienced observer who was blind to the patients' clinical information. A reversible perfusion defect was defined as a perfusion defect on the exercise images that partially or completely resolved at rest in at least two contiguous segments. A fixed perfusion defect was defined as a perfusion defect on exercise images, which persists on rest images. To assess the severity of perfusion abnormalities, the left ventricular myocardium was divided into 6 segments: anterior, inferior, septal anterior, septal posterior, posterolateral, and apical. Each of the 6 major left ventricular segments was scored using a 4-point scoring method (0 = normal, 1 = slightly reduced, 2 = moderately reduced, and 3 = severely reduced or absent uptake). The extent of myocardial ischemia on stress SPECT was defined by the number of segments with reversible or partially reversible perfusion defects. Low ischemia burden was defined as the presence of reversible perfusion abnormalities in <3 segments, whereas moderate to high ischemia burden was defined as ≥ 3 ischemic segments on SPECT.[7]

Follow-up

Outcome data were obtained by a questionnaire, evaluation of hospital records, contacting the patient's general practitioner, and/or review of civil registries. The online municipal civil registry was used to determine the patient's present survival status. The date of response was used to calculate follow-up time. The endpoints considered were all-cause mortality and cardiac mortality. Causes of death were obtained from the Central Bureau of Statistics Netherlands (www.cbs.nl). A death caused by acute MI, significant arrhythmias, refractory heart failure, or sudden death without other explanation was defined as cardiac mortality.

Statistical Analysis

Statistical analysis was performed using SPSS version 22 (IBM, Armonk, New York). Continuous data are expressed as mean ± SD and percentages are rounded. Continuous variables were compared with Student's t test for unpaired samples. Differences between proportions were compared with the chi-squared test. Logistic regression analysis was used to develop a propensity score to summarize predictors of the decision of referral to revascularization. Variables known to influence the decision to referral for revascularization were considered for entry in the logistic regression. This approach was followed by incorporating the propensity score as a covariate in the multivariable regression model. Kaplan-Meier survival curves were performed and were compared using the log-rank test. The impact of early coronary revascularization on survival was investigated using univariable and multivariable Cox's proportional hazard regression models. The multivariable model was performed using known prognostic factors, including cardiac risk factors, stress SPECT results, and the propensity score. Linearity of the relationship between covariates and survival in the Cox regression model was assessed using the martingale residuals. Plots of the residuals against the predicted values showed linearity and homoscedasticity. The assumption of the proportional hazards was evaluated by performing the log-minus-log survival plot; the assumption was met. To investigate collinearity, interaction terms were used; no interactions were observed. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95% confidence interval (95% CI). $P < .05$ was considered statistically significant.

RESULTS

Patient Characteristics

The 538 patients with myocardial ischemia on stress SPECT are characterized in Table 1. Mean age and mean body mass index (BMI) were 59.8 ± 11 years and 26.8 ± 4.4, respectively. A total of 395 (73%) patients were men. Regarding stress testing, 220 patients (41%) underwent exercise bicycle stress and 318 patients (59%) underwent dobutamine stress. Typical angina occurred in 150 patients (28%), whereas 176 patients (33%) exhibited ST-segment changes.

All patients had myocardial ischemia (defined as reversible or partially reversible perfusion defect) on stress SPECT. Fixed defects were observed in 81 (15%) patients. Both fixed and reversible defects were present in 344 (64%) patients. A total of 348 patients (65%) had low ischemia burden and 190 patients (35%) had moderate to high ischemia burden. A total of 76 (14%) patients underwent early revascularization (≤90 days after the stress SPECT); PCI was performed in 53 (70%) patients, and CABG was performed in 27 (36%) patients. A total of 4 patients (5%) underwent both PCI and CABG. The remaining 462 patients with myocardial ischemia on stress SPECT were treated only with pharmacologic therapy. Among the 76 patients who underwent early revascularization, mean number of abnormal segments was 2.5 ± 1.2 compared to 2.1 ± 1.1 in patients without early revascularization ($p = 0.005$). Patient groups were comparable according to age, BMI, smoking, hypertension, hypercholesterolemia, heart failure, diabetes mellitus, and previous MI (Table 1). Comparison of the patient groups shows that the patients who underwent early coronary revascularization were more frequent men, had more prior revascularization, and had more moderate to high ischemia burden. These factors may have contributed to referring for early coronary revascularization.

Long-Term Outcomes

During a median follow-up of 12 years (range 4-17), a total of 283 (53%) patients died (all-cause mortality) of whom 125 (44%) were due to cardiac causes. Kaplan-Meier survival curves are demonstrated in Figures 2, 3, 4, 5, and 6. Survival curves showed that patients with myocardial ischemia on stress SPECT who underwent early revascularization had a lower risk for all-cause mortality (event-free survival: 88 vs 72% at 5 years, 79 vs 55% at 10 years, 65 vs 44% at 15 years; overall $P < .001$, Figure 2) and cardiac mortality (event-free survival: 93 vs 82% at 5 years, 88 vs 76% at 10 years, 83 vs 72% at 15 years; overall $P = .03$, Figure 3). As Figures 4 and 5 shows, this lower risk was not influenced by the 348 patients with low ischemia burden (all-cause mortality, $P = .10$, Figure 4, and cardiac mortality, $P = .32$, Figure 5). In contrast, in the 190 patients with moderate to high ischemia burden, early revascularization was associated with better long-term outcomes compared to patients without early revascularization (all-cause mortality, $P < .001$, Figure 4; cardiac mortality, $P = .03$, Figure 5). Figure 6 shows Kaplan-Meier curves for the endpoint of cardiac mortality in patients who underwent early revascularization stratified to involvement of the left anterior descending artery (LAD). Of the 76 patients who underwent early revascularization, involvement of the LAD was associated with worse long-term outcomes compared to patients without LAD involvement.

Patients who were able to perform exercise bicycle testing had a better prognosis as compared with the patients who underwent dobutamine stress testing. In patients who underwent early revascularization, all-cause mortality was significantly higher in the dobutamine group than in the exercise group (Figure 7).

Univariable and Multivariable Predictors of Outcome

Logistic regression identified prior revascularization, male gender, and number of abnormal segments on SPECT as the best predictors of referral to revascularization ($P < .05$). Univariable and multivariable predictors of long-term outcome are presented in Tables 2 and 3, respectively. Univariable predictors of all-cause mortality were age, male gender, hypertension, diabetes mellitus, hypercholesterolemia, heart failure, prior MI, and number of abnormal segments on SPECT (Table 2). Univariable predictors of cardiac mortality were age, hypertension, diabetes mellitus, heart failure, previous MI, and number of abnormal segments on SPECT (Table 2). The univariable analysis also demonstrated that early revascularization was inversely related to both endpoints of interest.

The results of the multivariable analysis are shown in Table 3. Age, male gender, hypertension, diabetes mellitus, hypercholesterolemia, smoking, heart failure, previous revascularization, propensity score, and a number of abnormal segments on SPECT were associated with all-cause mortality (Table 3). Multivariable

Table 1. Clinical characteristics of 538 patients with reversible perfusion defects

Value (%)	All (*N* = 538)	Early revascularization (*N* = 76)	No early revascularization (*N* = 462)	*P* value
Age	59.8 ± 11	59.8 ± 9	59.8 ± 11	.96
Male gender	395 (73)	64 (84)	331 (72)	.02
BMI	26.8 ± 4.4	26.9 ± 3.4	26.9 ± 4.5	.99
Cardiac risk factors				
Smoking	158 (29)	23 (30)	135 (29)	.85
Hypertension	215 (40)	28 (37)	187 (40)	.55
Hypercholesterolemia	188 (35)	31 (41)	157 (34)	.25
Heart failure	82 (15)	9 (12)	73 (16)	.37
Diabetes mellitus	84 (16)	11 (14)	73 (16)	.77
Previous revascularization	161 (30)	34 (45)	127 (27)	.002
Previous MI	223 (41)	37 (49)	186 (40)	.17
Medications				
ACE-inhibitors	156 (29)	22 (38)	134 (29)	.99
Beta blockers	243 (45)	53 (70)	191 (41)	<.001
Calcium-channel blockers	209 (39)	43 (57)	166 (36)	<.001
Diuretics	116 (22)	10 (13)	106 (23)	.06
Nitrates	188 (35)	32 (42)	156 (34)	.16
Stress type				
Exercise bicycle	220 (41)	42 (55)	178 (39)	.01
Dobutamine	318 (59)	34 (45)	284 (61)	.01
SPECT parameters				
Number of abnormal segments	2.2 ± 1.5	2.5 ± 1.2	2.1 ± 1.1	.005
Low ischemia burden*	348 (65)	38 (50)	310 (67)	.004
Moderate to high ischemia burden*	190 (35)	38 (50)	152 (33)	.004

Values are expressed as means ± SD or numbers (%)
BMI, body mass index; *MI*, myocardial infarction; *ACE*, angiotensin-converting-enzyme; *SPECT*, single-photon emission computed tomography
* Low ischemia burden = 1 or 2 abnormal segments. Moderate to high ischemia burden = ≥3 abnormal segments

predictors of cardiac mortality were age, male gender, diabetes mellitus, and heart failure (Table 3). The multivariable Cox regression model revealed that early revascularization had a beneficial effect on both all-cause mortality (HR 0.46, 95% CI 0.30-0.69) and cardiac mortality (HR 0.54, 95% CI 0.29-0.99).

DISCUSSION

The present study evaluated the impact of early revascularization (≤90 days after stress SPECT) on long-term outcome in patients with myocardial ischemia on stress SPECT. Of the 538 patients, 30% of patients had previous revascularization and 41% had previous MI. During a median follow-up of 12 years, a total of 283 (53%) patients died (all-cause mortality) of whom 125 (44%) were due to cardiac causes. Kaplan-Meier survival curves showed that early revascularization (either PCI or CABG) after an ischemic stress SPECT was beneficial on both all-cause mortality and cardiac mortality. In patients with low ischemia burden on stress SPECT (defined as <3 ischemic segments), early revascularization was not associated with better long-term outcomes, whereas in patients with moderate to severe ischemia burden (defined as ≥3 ischemic segments), early revascularization was associated with better long-

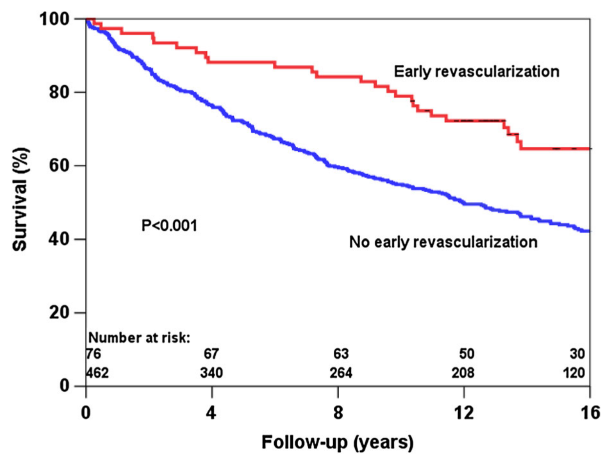

Figure 2. Kaplan-Meier curves for all-cause mortality according to strata of early coronary revascularization.

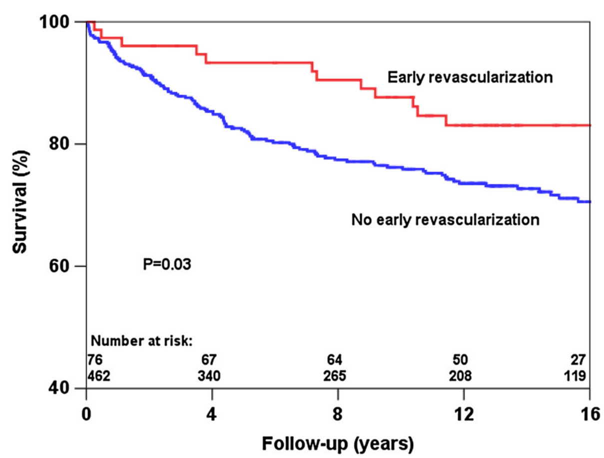

Figure 3. Kaplan-Meier curves for cardiac mortality according to strata of early coronary revascularization.

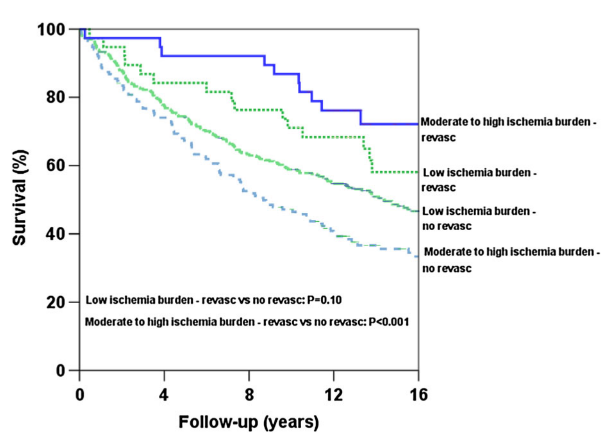

Figure 4. Kaplan-Meier curves for all-cause mortality according to strata of the extent of ischemia (low ischemia burden vs moderate to high ischemia burden) and early coronary revascularization (revasc vs no revasc).

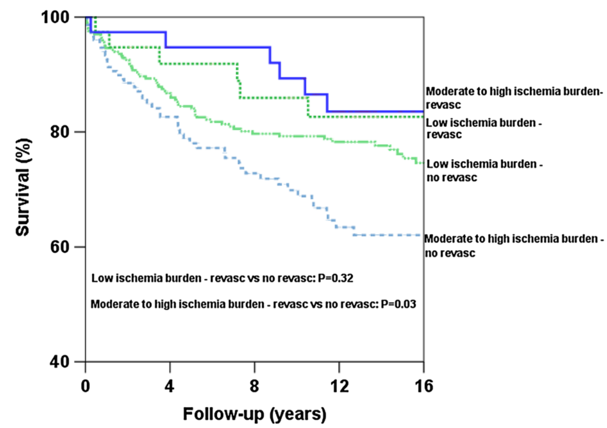

Figure 5. Kaplan-Meier curves for cardiac mortality according to strata of the extent of ischemia (low ischemia burden vs moderate to high ischemia burden) and early coronary revascularization (revasc vs no revasc).

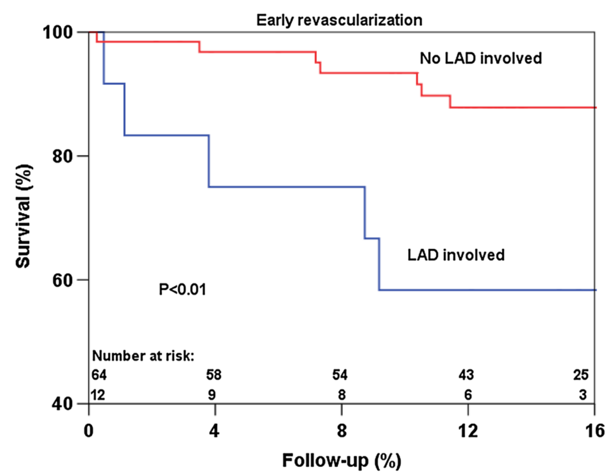

Figure 6. Kaplan-Meier survival curves for the endpoint of cardiac mortality in patients who underwent early revascularization stratified to involvement of the left anterior descending artery (LAD) (LAD vs no LAD involved).

term outcomes. The multivariable model demonstrated that early revascularization was associated with a 54% reduction in all-cause mortality and a 46% reduction in cardiac mortality. Also, in patients who underwent early revascularization without involvement of the LAD, cardiac mortality was lower compared to patients who were revascularized with involvement of the LAD. Regarding the type of stress test, patients with early revascularization who performed a dobutamine stress test had higher all-cause mortality compared to patients who performed exercise bicycle stress testing. This finding is in accordance with a previous report from our center.[10] The inability to perform exercise testing is a negative prognostic marker in patients with CAD.

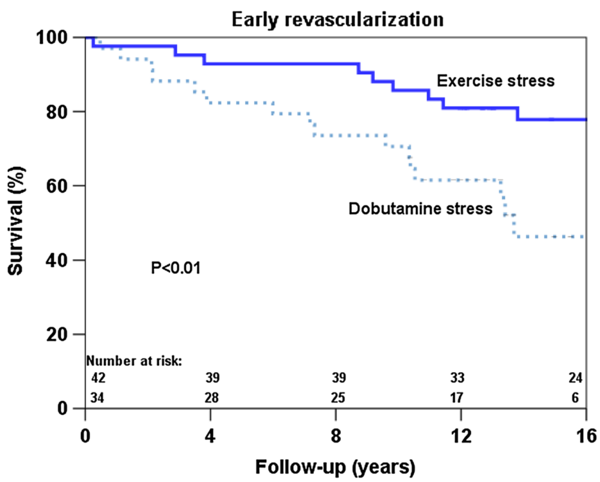

Figure 7. Kaplan-Meier survival curves for the endpoint of all-cause mortality in patients who underwent early revascularization stratified to stress type (exercise test vs dobutamine stress test).

In recent years, there has been a considerable interest concerning treatment strategies in patients with stable CAD resulting in a wealth of published literature. Both revascularization (PCI and/or CABG) and optimal medical therapy are treatment options in these patients. SPECT MPI plays a central role in this regard. To date, information on long-term outcomes after revascularization in relation to the ischemia burden on stress SPECT is relatively scarce. Previous studies have examined the short-term to medium-term outcomes after revascularization in patients with ischemia on SPECT. Hachamovitch et al[3] studied >10.000 patients without previous MI and without previous revascularization who underwent stress SPECT. The study population was divided in patients who were treated medically and patients who underwent early revascularization and was followed during a mean follow-up of 1.9 years. In patients with moderate to severe ischemia (>10% myocardial ischemia), revascularization was associated with improved survival in comparison to medical therapy. Sorajja et al[11] evaluated 826 asymptomatic diabetic patients without known CAD who underwent exercise, adenosine, or dobutamine stress SPECT. SPECT images were classified as low, intermediate, and high risk. A total of 261 patients (32%) had a high-risk SPECT (defined as a summed stress score ≤47, based on: the lower the score the higher the radioisotope uptake). During a mean follow-up of 5.7 ± 3.3 years, CABG was associated with better survival in patients with moderate to severe ischemia. The current study differs from these previous studies for several reasons. First, the current study evaluated a high-risk patient group (30% had previous revascularization and 41% had previous MI vs 0% in the studies of Hachamovitch et al and Sorajja et al). Second, this study showed higher event rates. This may be explained by the high prevalence of cardiac history indicating a higher risk status in contrast to these previous studies. Also, during the current long-term follow-up natural progression of CAD may have occurred. Third, the mean follow-up duration in these previous studies was 1.9 and 5.7 years. In the present long-term follow-up study, median follow-up duration was 12 years. To our knowledge, this is the first study that has examined the impact of early revascularization in relation the amount of ischemia in patients with stable CAD for long-term (>10 years) outcome.

Table 2. Univariable predictors of all-cause mortality and cardiac mortality

Variable	All-cause mortality HR	All-cause mortality 95% CI	Cardiac mortality HR	Cardiac mortality 95% CI
Age*	1.06	1.04-1.07	1.06	1.04-1.07
Male gender	1.34	1.09-1.77	1.29	0.85-1.97
Hypertension	1.57	1.24-1.98	1.60	1.12-1.27
Diabetes mellitus	2.47	1.87-3.27	3.14	2.13-4.62
Hypercholesterolemia	0.67	0.52-0.87	0.70	0.48-1.03
Smoking	1.04	0.80-1.34	0.96	0.65-1.42
Heart failure	2.34	1.79-3.18	2.99	2.01-4.45
Previous revascularization	1.08	0.84-1.38	1.19	0.82-1.73
Previous MI	1.46	1.15-1.84	1.69	1.19-2.41
# abnormal segments on SPECT	1.13	1.02-1.24	1.20	1.04-1.39
Early revascularization	0.46	0.30-0.69	0.52	0.29-0.95

* Per unit increment
#, number; *MI*, myocardial infarction; *SPECT*, single-photon emission computed tomography

Table 3. Multivariable predictors of all-cause mortality and cardiac mortality

Variable	All-cause mortality		Cardiac mortality	
	HR	95% CI	HR	95% CI
Age*	1.07	1.05–1.08	1.06	1.04–1.09
Male gender	1.95	1.40–2.71	1.80	1.10–2.93
Hypertension	1.31	1.02–1.68	1.22	0.84–1.77
Diabetes mellitus	2.42	1.78–3.28	2.96	1.94–4.54
Hypercholesterolemia	0.76	0.58–0.99	0.79	0.53–1.18
Smoking	1.52	1.15–2.00	1.41	0.93–2.14
Heart failure	1.35	1.97–1.88	1.60	1.00–2.56
Previous revascularization	1.45	1.04–2.03	1.56	0.95–2.57
Previous MI	1.08	0.82–1.41	1.20	0.81–1.80
Propensity score	0.04	0.01–0.50	0.05	0.00–1.83
# abnormal segments on SPECT	1.19	1.03–1.38	1.23	0.99–1.52
Early revascularization	0.46	0.30–0.69	0.54	0.29–0.99

* Per unit increment
#, number; *MI*, myocardial infarction; *SPECT*, single-photon emission computed tomography

This study extends the conclusions drawn from these previous studies in that early revascularization in patients with moderate to high ischemia burden is beneficial during long-term outcome. The current findings are also in line with previous data which indicates that a certain amount of ischemia has to be present for revascularization to be beneficial.[12]

In a nuclear substudy of the COURAGE trial,[6] a total of 314 patients were enrolled who underwent either exercise or vasodilator stress ^{99m}Tc-sestamibi SPECT. Moderate to severe ischemia on SPECT was defined as $\geq$10% myocardium. The authors found that the magnitude of residual ischemia was proportional to the risk of all-cause mortality. However, as the authors noted, these findings are based on underpowered data due to the small proportion of enrolled patients.[6] More recently, a second nuclear substudy of the COURAGE trial was performed.[7] Of the 1381 patients who underwent SPECT, 699 patients were treated medically and 682 patients received medical treatment and PCI. Patients were followed for a median follow-up of 4.6 years. The extent of ischemia was not associated with adverse events; the event rates in both mild ischemia and moderate-severe ischemia were similar according to treatment options (medical treatment or medical treatment combined with PCI). In the current long-term follow-up study, early revascularization was associated with lower all-cause mortality and cardiac mortality.

There are several differences between the current study and the COURAGE nuclear substudies.[6,7] First, the present study demonstrates that survival was significantly different between patients with revascularization and those without during a median follow-up duration of 12 years. The maximum follow-up duration in the previous trials was approximately 5 years. Second, while the previous mentioned trials enrolled mainly low to intermediate risk patients, the current study describes a high-risk group of patients who were unable to perform an exercise test. Third, 41% of the 538 patients (vs 38%) had a previous myocardial infarction and 82 (15%) patients (vs 4.7%) had known heart failure compared to the COURAGE trial. Finally, in contrast to the previous trials which had a randomized design, the current study is of retrospective observational design with inherent limitations. However, the current study describes 'physician—selected' patients which are commonly encountered in with daily practice; all of these factors may have influenced the beneficial effect of early coronary revascularization in this high-risk group of patients.

NEW KNOWLEDGE GAINED

In patients with myocardial ischemia on stress SPECT, early coronary revascularization is associated with lower all-cause mortality and cardiac mortality during long-term follow-up (>10 years) as compared to patients who received pharmacological therapy only.

LIMITATIONS

This study has several limitations. First, the decision to perform coronary revascularization was made by the treating physician, this could have influenced the results. Although the current study was of observational design—in contrast to the COURAGE nuclear substudies[6,7]—we tried to avoid bias for referral to revascularization using a propensity score. However, limitations inherent of the observational design, like missing covariates cannot be ignored. Because this is a nonrandomized observational study, the results should be interpreted with caution and should be viewed in conjunction with the results from randomized trials. Second, at time of data collection, medications were underused in view of the current treatment guidelines, maybe because the beneficial effect of these medications was not yet fully understood.[13] Third, the use of a 6-segment myocardial model is less accurate compared to the standard 17-segment myocardial model. However, this strategy has been previously described in literature.[7] This could have influenced the outcome. Fourth, the patient population was relatively small. This may have influenced the results. Finally, the prognostic value of gated SPECT was not examined, due to the fact that at the time of data collection-gated SPECT was not routinely performed in our center. As a result left ventricular ejection fraction (LVEF) was not available. Information about LVEF could have improved the analysis of the current study.

CONCLUSION

Patients with myocardial ischemia on stress SPECT who underwent early revascularization had a lower all-cause mortality and cardiac mortality during long-term follow-up as compared to patients who received pharmacological therapy alone. This difference in long-term outcomes was mainly influenced by the survival benefit of early revascularization in the patients with a moderate to high ischemia burden. In patients with low ischemia burden, early coronary revascularization had no beneficial impact on long-term outcomes as compared to a treatment strategy based on pharmacological therapy alone.

Disclosure

All authors declare no conflicts of interest.

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