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Impact of the Charlson Comorbidity Index score on risk prediction by single-photon emission computed tomography myocardial perfusion imaging following myocardial infarction

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Background: Comorbidity is common among patients with myocardial infarction (MI). We examined whether comorbidity level modified the single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI)-based prediction of 5-year risk of MI and all-cause death in patients with MI.

Methods: This cohort study included patients with prior MI having a SPECT MPI at Aarhus University Hospital, Denmark, 1999–2011. Using nationwide registries, we obtained information on comorbidity levels (low, moderate, and severe) and outcomes. We computed risk and hazard ratios (HRs) with 95% confidence intervals (CIs) for MI and all-cause death, comparing normal (no defects) versus abnormal scan (reversible and/or fixed defects) using Cox regression adjusting for sex, age, and comorbidity level.

Results: We identified 1,192 patients with MI before SPECT MPI. The 5-year risk for patients with normal versus abnormal scans were 11.7% versus 18.3% for MI, and 8.0% versus 13.2% for all-cause death, respectively. The overall 5-year adjusted HR (aHR) of MI was 1.56 (95% CI: 1.09–2.21), 1.33 (95% CI: 0.82–2.15) with low comorbidity, 1.39 (95% CI: 0.68–2.83) with moderate comorbidity, and 2.53 (95% CI: 1.14–5.62) with severe comorbidity. Similarly, the 5-year aHR for all-cause death was 1.39 (95% CI: 0.90–2.14) overall; 2.33 (95% CI: 0.79–6.84) with low comorbidity, 2.05 (95% CI: 0.69–6.06) with moderate comorbidity, and 1.07 (95% CI: 0.64–1.80) with severe comorbidity.

Conclusion: We conclude that comorbidity level may modify the 5-year risk prediction associated with an abnormal SPECT MPI scan in patients with previous MI.

Keywords: comorbidity, epidemiology, myocardial infarction, myocardial perfusion imaging

Introduction

Single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI) is a non-invasive procedure for risk stratification after myocardial infarction (MI).^{1,2} With increasing age, the number of patients with chronic disorders are increased.³ Concurrently, life expectancy among MI patients has increased during recent decades due to improvements in treatment and rehabilitation.^{4,5} Consequently, more MI patients have other chronic diseases, i.e. comorbidities.⁶ The prevalence of comorbidity among MI patients may be increased further due to shared risk factors between cardiovascular disease and other diseases, such as diabetes.⁷

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It has previously been shown that comorbidity level did not affect substantially the association between SPECT MPI scan result and the risk of MI and all-cause death in patients without previous MI or cerebrovascular disease.⁸ Despite the common presence of comorbid conditions in MI patients, the impact of comorbidity level on the prognosis following a normal versus abnormal SPECT MPI scan in MI patients has to our knowledge not previously been examined. We therefore examined the SPECT MPI-predicted 5-year risk of MI and all-cause death following a normal versus abnormal SPECT MPI scan in patients with previous MI, both overall and according to comorbidity level.

Methods

Setting

The Danish National Health Service provides free universal tax-supported healthcare, guaranteeing unfettered access to general practitioners and hospitals.⁹ Using the unique 10-digit Civil Personal Register number assigned to each individual who was born in or immigrated to Denmark, it is possible to link all Danish medical registries at the individual level.¹⁰

Study population

We conducted this cohort study in Denmark using the Aarhus University Hospital Myocardial Perfusion Imaging (AUH-MPI) Database.⁸ According to a previously published paper, this database has collected information on all ^{99m}Tc-sestamibi SPECT MPI procedures performed at Aarhus University Hospital, Skejby, Denmark from January 1999 until April 2011, and contains information on sex, age, and scan result.⁸ We used the AUH-MPI Database to identify all adult Danish patients (over the age of 18 years) who had a ^{99m}Tc-sestamibi SPECT MPI procedure performed between January 1999 and April 2011. To be eligible for inclusion in this study, patients should have a first-time MI diagnosis within 5 years before the SPECT MPI procedure date, as ascertained from the Danish National Patient Registry (DNPR). The DNPR has recorded information on patients discharged from all non-psychiatric hospitals in Denmark since 1977 and from emergency room and outpatient clinic visits since 1995.¹¹ One primary diagnosis and up to 19 secondary diagnoses are provided for each hospital discharge or outpatient clinical visit, classified according to the International Classification of Diseases, 8th Revision

(ICD-8) until the end of 1993 and 10th Revision (ICD-10) thereafter.¹¹ We considered only the first SPECT MPI procedure in the study period for each patient.

The SPECT MPI procedure is performed by combining a stress and a rest scan to evaluate any signs of reversibility, irreversibility, or a combination of both. Stress is applied either physically on an ergometer bicycle or pharmacologically with vasodilating (adenosine or dipyridamole) or beta stimulating (dobutamine) drugs. A normal scan was defined as a scan without defects, and an abnormal scan was defined by the presence of a reversible and/or fixed defect.⁸ We further subdivided an abnormal scan into 3 groups: a reversible defect, a fixed defect, and a combined defect (reversible and fixed defect).

Outcomes

We used the DNPR¹¹ to identify all inpatient admissions and outpatient clinic contacts with a primary or secondary diagnosis of MI following a SPECT MPI procedure during the study period.

We used the Danish Civil Registration System¹⁰ to obtain information on all-cause mortality. This registry has recorded information on date of birth, residence, date of emigration, and exact date of any death for the entire Danish population since 1968, with daily electronic updates.¹⁰

Comorbidity

We obtained information on comorbid conditions from inpatient and outpatient hospital diagnoses recorded in the DNPR¹¹ between 1977 and the date of the SPECT MPI procedure. The severity of comorbidity was categorized using Charlson Comorbidity Index (CCI) scores.¹² CCI scores have been found to be a valid method for measuring comorbidity,¹³ also in MI patients.¹⁴ We computed the CCI score by summing the weight of the remaining 18 conditions included in the CCI after excluding MI. We then categorized the study population according to the following comorbidity levels: score of 0 (low comorbidity), score of 1 (moderate comorbidity), and score ≥ 2 (severe comorbidity).

Statistical analysis

We used descriptive statistics to characterize the study population undergoing SPECT MPI according to sex, age, comorbidity level, and cardiovascular morbidity (congestive heart failure, peripheral vascular disease, cerebrovascular disease, and diabetes). Follow-up began on the

date of the SPECT MPI procedure or discharge from the hospital admission during which the SPECT MPI procedure was performed. Follow-up continued until the date of MI, death, emigration, 5 years of follow-up, or November 15, 2013, whichever came first.

We used a cumulative incidence method to calculate the absolute risk and risk difference of MI and all-cause death within 30 days (including 0 days and 30 days), 31–365 days (including 31 days, and excluding 365 days), 1–5 years (including 1 year, and excluding 5 years), and 5 years over-all following SPECT MPI, and illustrated graphically the risk for all-cause death. Death was considered a competing risk in the analyses of MI.

We assessed the impact of comorbidity on risk of MI and all-cause death in MI patients following a normal versus abnormal SPECT MPI scan by stratifying the analyses by comorbidity level. We used Cox proportional hazards regression to compute 5-year hazard ratios (HRs) with 95% confidence intervals (CIs) for each outcome, comparing an abnormal scan with a normal scan, and adjusting for categories of sex, age (18–49 years, 50–59 years, 60–69 years, and ≥ 70 years), and comorbidity level (low, moderate, and severe comorbidity).

In addition, we conducted 3 sensitivity analyses. The first analysis restricted the outcome to MI diagnoses during an acute inpatient admission. The second and third analyses were restricted to patients diagnosed with a first-time MI 0–1 year and >1 –5 years before the SPECT MPI procedure, respectively, to examine the consistency of associations according to time from infarction. The proportional hazards assumption was assessed graphically by log(-log)-plots and found valid within the 0–5-year period. The ICD codes for conditions included in the CCI and for MI are provided in [Table S1](#) and [S2](#). All statistical analyses were conducted using Stata software 12.1 (StataCorp LP, College Station, Texas, USA).

Ethics statement

The study was approved by the Danish Data Protection Agency (record number 2015-57-0002; Aarhus University record number 2016-051-000001-509).

Results

Patient characteristics

We identified 1,192 patients with a first-time MI within 5 years before the SPECT MPI. Among these, 362 patients

(30%) had a normal scan and 830 patients (70%) had an abnormal scan ([Table 1](#)). Their sex and age distributions are shown in [Table 1](#). A total of 152 patients had reversible scan defects, 403 patients had fixed scan defects, and 275 patients had combined scan defects. Among patients with a normal scan, 54% had a low comorbidity level, and among patients with an abnormal scan, 44% had a low comorbidity level. The prevalence of patients with moderate comorbidity was nearly equally distributed among patients with normal and abnormal scans (25% versus 26%). Patients with a normal scan were less likely to have severe comorbidity than patients with an abnormal scan (21% versus 30%) ([Table 1](#)). Patients with a normal scan also were less likely to have had congestive heart failure than patients with an abnormal scan (9% versus 21%). The prevalence of peripheral vascular disease was very similar among patients with normal and abnormal scans (8% versus 9%) ([Table 1](#)). The prevalence of cerebrovascular disease and diabetes was lower among patients with a normal scan than among patients with an abnormal scan (8% versus 12%, and 12% versus 15%, respectively) ([Table 1](#)).

The median time from MI to SPECT MPI within the study cohort was 0.9 years (interquartile range (IQR): 0.3 years to 2.2 years).

Outcomes

Within 5 years after SPECT MPI, 190 MIs and 131 all-cause deaths occurred in the cohort ([Table 2](#)). Median follow-up time for all-cause death was 5 years (IQR: 4.6 years to 5 years), and for MI the median follow-up time was 5 years (IQR: 3.5 years to 5 years).

Five-year risk of MI was 11.7% (95% CI: 8.5–15.5) among patients with normal scans, and 18.3% (95% CI: 15.7–21.0) among patients with abnormal scans ([Table 2](#)). The corresponding adjusted HR (aHR) in the 5-year period was 1.56 (95% CI: 1.09–2.21) ([Table 2](#)). The overall 5-year risk difference is shown in [Table 2](#). Risk estimates within 0–30 days, 31–365 days, and 1–5 years following SPECT MPI are provided in [Table 3](#). Sensitivity analyses restricted to the 112 MI diagnoses during an acute admission supported the overall result, with aHR of 1.35 (95% CI: 0.86–2.12) ([Table 4](#)). Using a normal scan as the reference, the aHR for the 5-year period was 1.22 (95% CI: 0.72–2.07) for a reversible defect, 1.58 (95% CI: 1.07–2.33) for a fixed defect, and 1.72 (95% CI: 1.14–2.61) for a combined defect ([Table 5](#)). The sensitivity analyses that examined the consistency of associations according to time from MI to SPECT MPI supported the overall result with an

Table 1 Patients with normal and abnormal scans by sex, age, comorbidity level, and cardiovascular morbidity

Characteristics	Normal scan (n=362)	Abnormal scan (n=830)	Total (n=1,192)
Sex			
Female	165 (46%)	233 (28%)	398 (33%)
Male	197 (54%)	597 (72%)	794 (67%)
Age (years)			
18–49	69 (19%)	149 (18%)	218 (18%)
50–59	119 (33%)	236 (28%)	355 (30%)
60–69	95 (26%)	245 (30%)	340 (29%)
≥70	79 (22%)	200 (24%)	279 (23%)
Median age (years)	59	60	60
Comorbidity level*			
Low	195 (54%)	369 (44%)	564 (47%)
Moderate	89 (25%)	215 (26%)	304 (26%)
Severe	78 (21%)	246 (30%)	324 (27%)
Cardiovascular morbidity			
Congestive heart failure	34 (9%)	171 (21%)	205 (17%)
Peripheral vascular disease	30 (8%)	78 (9%)	108 (9%)
Cerebrovascular disease	30 (8%)	97 (12%)	127 (11%)
Diabetes	43 (12%)	126 (15%)	169 (14%)

Note: Included are patients with a first-time myocardial infarction within 5 years before the scan. *Levels of comorbidity were based on Charlson Comorbidity Index scores as follows: 0 (low), 1 (moderate), and ≥2 (severe).

aHR of 1.53 (95% CI: 0.95–2.47) for MI patients whose infarction occurred 0–1 year before SPECT MPI (Table S3), and 1.57 (95% CI: 0.93–2.65) for MI patients whose infarction occurred >1–5 years before SPECT MPI (Table S4).

Patients with a normal scan had a 5-year mortality risk of 8.0% (95% CI: 5.5–11.5). In patients with an abnormal scan, this risk was 13.2% (95% CI: 11.0–15.7) (Table 2). The corresponding aHR was 1.39 (95% CI: 0.90–2.14) (Table 2). The cumulative mortality risk is provided in Figure 1. The overall 5-year risk difference is shown in Table 2, and risk estimates within 0–30 days, 31–365 days, and 1–5 years following SPECT MPI are provided in Table 3.

Using a normal scan as reference, the aHR was 0.97 (95% CI: 0.51–1.85) for a reversible defect, 1.41 (95% CI: 0.87–2.27) for a fixed defect, and 1.61 (95% CI: 0.99–2.64) for a combined defect (Table 5). No substantial differences were seen in the aHRs in sensitivity analyses restricted to patients whose previous MI occurred 0–1 year before SPECT MPI (aHR =1.19; 95% CI: 0.65–2.17) (Table S3) or >1–5 years before SPECT MPI (aHR =1.56; 95% CI: 0.84–2.89) (Table S4), compared to the overall results.

Comorbidity

For all 3 levels of comorbidity, an abnormal scan was associated with an increased 5-year risk of MI compared with a normal scan, as well as considerable risk differences between patients with a normal versus abnormal scan (Table 2). Five-year aHRs comparing an abnormal scan with a normal scan were 1.33 (95% CI: 0.82–2.15) among patients with low comorbidity, 1.39 (95% CI: 0.68–2.83) among patients with moderate comorbidity, and 2.53 (95% CI: 1.14–5.62) among patients with severe comorbidity (Table 2).

Compared with a normal scan, an abnormal scan was associated with an increased 5-year risk of all-cause death among patients with all 3 levels of comorbidity (Table 2). Risk differences according to comorbidity levels were 3.7% (95% CI: 0.5–6.8) for low comorbidity, 5.1% (95% CI: -1.5–11.6) for moderate comorbidity, and 0.8% (95% CI: -10.9–12.4) for severe comorbidity (Table 2). Comparing an abnormal scan with a normal scan, the 5-year aHR was 2.33 (95% CI: 0.79–6.84) among patients with low comorbidity, 2.05 (95% CI: 0.69–6.06) among patients with moderate comorbidity, and 1.07 (95% CI: 0.64–1.80) among patients with severe comorbidity (Table 2).

Table 2 Risk and hazard ratio of MI and all-cause death within 5 years following a normal versus abnormal scan, overall and according to comorbidity level

Outcome	Scan result	No. of events	Risk % (95% CI)	Risk difference % (95% CI)	Hazard ratio (95% CI)	
					Unadjusted	Adjusted*
Overall						
MI	Normal	41	11.7 (8.5 – 15.5)	6.6 (2.1 – 11.1)	I (reference)	I (reference)
	Abnormal	149	18.3 (15.7 – 21.0)		1.64 (1.16 – 2.31)	1.56 (1.09 – 2.21)
All-cause death	Normal	27	8.0 (5.5 – 11.5)	5.2 (1.4 – 8.9)	I (reference)	I (reference)
	Abnormal	104	13.2 (11.0 – 15.7)		1.66 (1.09 – 2.54)	1.39 (0.90 – 2.14)
Low comorbidity (0 points)						
MI	Normal	24	12.6 (8.1 – 18.1)	4.5 (–1.9 – 10.9)	I (reference)	I (reference)
	Abnormal	62	17.1 (13.4 – 21.2)		1.41 (0.88 – 2.25)	1.33 (0.82 – 2.15)
All-cause death	Normal	4	2.1 (0.8 – 5.4)	3.7 (0.5 – 6.8)	I (reference)	I (reference)
	Abnormal	20	5.7 (3.7 – 8.8)		2.64 (0.90 – 7.72)	2.33 (0.79 – 6.84)
Moderate comorbidity (1 point)						
MI	Normal	10	12.0 (6.1 – 20.0)	4.6 (–4.2 – 13.3)	I (reference)	I (reference)
	Abnormal	35	16.5 (11.9 – 21.8)		1.45 (0.72 – 2.93)	1.39 (0.68 – 2.83)
All-cause death	Normal	4	5.2 (2.0 – 13.5)	5.1 (–1.5 – 11.6)	I (reference)	I (reference)
	Abnormal	21	10.3 (6.8 – 15.4)		2.04 (0.70 – 5.96)	2.05 (0.69 – 6.06)
Severe comorbidity (≥2 points)						
MI	Normal	7	9.0 (4.0 – 16.7)	12.6 (3.8 – 21.4)	I (reference)	I (reference)
	Abnormal	52	21.6 (16.7 – 27.1)		2.48 (1.13 – 5.45)	2.53 (1.14 – 5.62)
All-cause death	Normal	19	25.9 (17.3 – 37.7)	0.8 (–10.9 – 12.4)	I (reference)	I (reference)
	Abnormal	63	26.6 (21.5 – 32.8)		1.03 (0.62 – 1.72)	1.07 (0.64 – 1.80)

Note: Included are patients with a first-time MI within 5 years before the scan. *Adjusted for sex, age, and comorbidity level in the overall analyses, and sex and age in the analyses stratified on comorbidity level.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

Discussion

In this cohort study of patients with previous MI, we found that comorbidity level may modify the 5-year risk prediction of an abnormal SPECT MPI scan for MI and all-cause death. The impact of an abnormal scan was strongest for MI in patients with severe comorbidity. For all-cause death, the impact of an abnormal scan was strongest in patients with low and moderate comorbidity.

An important study strength was access to a study population in a setting of a universal free tax-supported health care system. All Danish citizens have universal and free access to general practitioners and hospitals, which minimizes selection bias. Another study strength is complete follow-up of all patients until the date of an outcome, emigration, or end of follow-up.¹¹ Information about the SPECT MPI scan result was obtained before the information on the outcomes. Furthermore, recorded diagnoses in the DNPR are likely to be independent of the SPECT MPI

scan result. Any potential misclassification therefore would be non-differential and cannot explain the increased aHRs for MI and all-cause death.

We cannot entirely rule out that some patients with a SPECT MPI scan in the study period were not registered in the AUH-MPI Database. However, we assume that the association between SPECT MPI and outcomes among unregistered patients would not differ from those among registered patients. This should, therefore, not have influenced our results.

The positive predictive values of MI diagnoses and comorbidities included in the CCI have been reported to be high in the DNPR; 97% for first-time MI,¹⁵ 98% for CCI comorbidities,¹⁶ and 88% for an inpatient diagnosis of recurrent MI.¹⁵ Mortality data from the Danish Civil Personal Registration System are complete.¹⁰ We controlled for other potential predictors (sex, age, and comorbidity level). However, it is possible that other unmeasured variables, such

Table 3 30-day, 31–365-day, and 1–5-year risk of MI and all-cause death following a normal versus abnormal scan

Time intervals	Scan result	No. of events	Risk % (95% CI)	Risk difference % (95% CI)
0–30 days				
MI	Normal	7	1.7 (0.6 – 3.6)	−0.1 (−1.8 – 1.6)
	Abnormal	14	1.6 (0.9 – 2.6)	
All-cause death	Normal	1	0.3 (0.0 – 1.9)	−0.2 (−0.8 – 0.4)
	Abnormal	1	0.1 (0.0 – 0.9)	
31–365 days				
MI	Normal	15	4.0 (2.2 – 6.5)	3.3 (0.5 – 6.1)
	Abnormal	60	7.2 (5.6 – 9.2)	
All-cause death	Normal	6	1.7 (0.8 – 3.7)	0.9 (−0.8 – 2.6)
	Abnormal	21	2.5 (1.7 – 3.9)	
1–5 years				
MI	Normal	19	6.5 (4.0 – 9.7)	4.1 (0.3 – 7.9)
	Abnormal	75	10.6 (8.4 – 13.0)	
All-cause death	Normal	20	6.2 (4.0 – 9.5)	4.6 (1.1 – 8.0)
	Abnormal	82	10.8 (8.8 – 13.2)	

Note: Included are patients with a first-time MI within 5 years before the scan.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

Table 4 Risk and hazard ratio of MI registered during an acute admission within 5 years following a normal versus abnormal scan

Outcome	Scan result	No. of events	Risk % (95% CI)	Hazard ratio (95% CI)	
				Unadjusted	Adjusted*
MI	Normal	25	7.0 (4.6 – 10.2)	1 (reference)	1 (reference)
	Abnormal	87	10.8 (8.8 – 13.1)	1.54 (0.98 – 2.40)	1.35 (0.86 – 2.12)

Note: Included are patients with a first-time MI within 5 years before the scan. *Adjusted for sex, age, and comorbidity level.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

Table 5 Risk and hazard ratio of MI and all-cause death within 5 years following a normal scan, a reversible defect, a fixed defect, and a combined defect. Included are patients with a first-time MI within 5 years before the scan

Outcome	Scan result	No. of events	Risk % (95% CI)	Hazard ratio (95% CI)	
				Unadjusted	Adjusted*
MI	Normal	41	11.7 (8.5 – 15.5)	1 (reference)	1 (reference)
	Reversible defect	21	14.1 (9.1 – 20.2)	1.25 (0.74 – 2.11)	1.22 (0.72 – 2.07)
	Fixed defect	74	18.4 (14.7 – 22.4)	1.67 (1.14 – 2.44)	1.58 (1.07 – 2.33)
	Combined defect	54	20.1 (15.5 – 25.1)	1.81 (1.21 – 2.72)	1.72 (1.14 – 2.61)
All-cause death	Normal	27	8.0 (5.5 – 11.5)	1 (reference)	1 (reference)
	Reversible defect	14	9.7 (5.9 – 15.9)	1.21 (0.64 – 2.31)	0.97 (0.51 – 1.85)
	Fixed defect	49	12.6 (9.7 – 16.3)	1.61 (1.00 – 2.57)	1.41 (0.87 – 2.27)
	Combined defect	41	15.9 (11.9 – 21.0)	2.00 (1.23 – 3.25)	1.61 (0.99 – 2.64)

Note: *Adjusted for sex, age, and comorbidity level.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

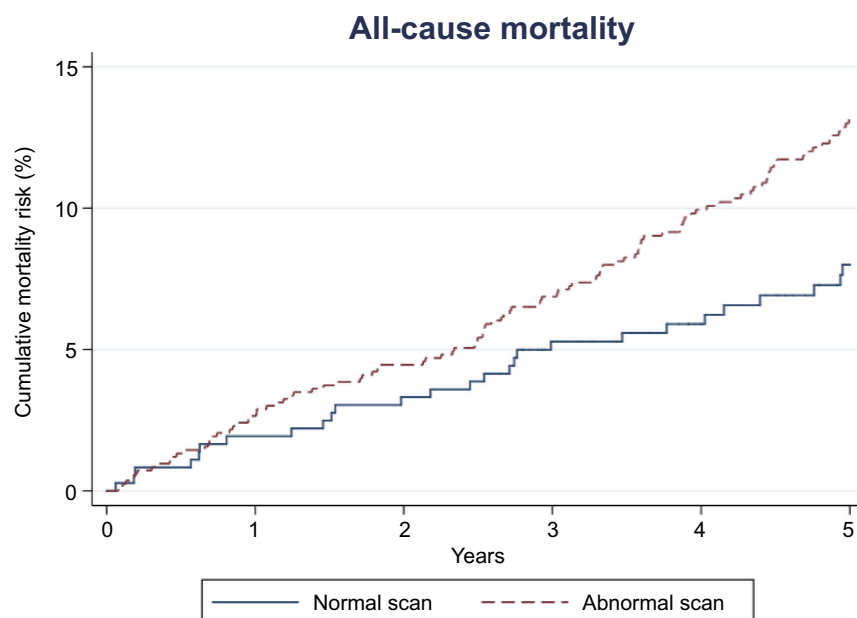


Figure 1 Estimated cumulative incidence of all-cause mortality risk among patients with normal and abnormal scans.

as smoking, hypertension, and obesity, influenced the results. Nevertheless, our primary aim was to assess the predictive ability of SPECT MPI, rather than to examine a possibly causal relation, in which confounding would have been an issue.

Our study was of limited size. Thus, some of our estimates were imprecise and with broad CIs, and we cannot rule out that some of our findings are due to chance. Finally, as we only included MI patients with a SPECT MPI scan, we cannot generalize our findings to MI patients without a SPECT MPI scan.

To our knowledge, no other studies have examined the risk of MI and all-cause death as separate outcomes following an abnormal versus normal SPECT MPI scan in MI patients, but previous studies have examined the risk of MI or death as combined endpoints after MI following SPECT.^{17,18} A study by Jain et al¹⁷ examined the risk of death or reinfarction following dipyridamole thallium testing 3 to 21 days after acute MI with a median follow-up of 18 months in 73 patients aged 65 years and older (mean age 75 years). The authors reported that reversible ischemia was a predictor of death or reinfarction, with a relative risk of 2.51 (95% CI: 1.05–5.96). Stratmann et al¹⁸ examined the risk of late cardiac events (non-fatal MI or cardiac death) in 133 men hospitalized with an acute MI who had technetium-99m sestamibi SPECT before hospital discharge. The mean time to a cardiac event after testing was 19 months, and in those patients without an event,

follow-up was 39 months. The study found that an isolated fixed defect was a predictor of increased risk for late cardiac events (relative risk of 2.1; 95% CI: 1.1–4.3).

These above-mentioned studies used combined endpoints. Therefore, their results are not completely comparable with our study's results.

The impact of comorbidity level on risk of MI and all-cause death following a normal versus abnormal SPECT MPI scan has to our knowledge not previously been investigated in patients with MI. Rather, earlier studies examined the risk of adverse events following a normal versus abnormal SPECT MPI in patients with selected chronic conditions, including diabetes, obesity, and end-stage renal disease.^{19–21} These studies looked at specific chronic conditions rather than different comorbidity levels, and did not restrict their study population to previous MI patients. Their results are therefore not comparable with ours.

Conclusion

In conclusion, comorbidity level may modify the 5-year risk prediction of an abnormal SPECT MPI scan in patients with previous MI. The impact of an abnormal scan was strongest for MI in patients with severe comorbidity, and for all-cause death in patients with low and moderate comorbidity. When SPECT MPI is used as a prognostic tool, the difference in its predictive value across comorbidity levels should be considered.

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Supplementary materials

Table S1 Diagnosis codes according to the International Classification of Diseases, 8th (ICD-8) and 10th revision (ICD-10)

Disease	Weight	ICD-8 codes	ICD-10 codes
Myocardial infarction	1	410	I21, I22, I23
Congestive heart failure	1	427.09, 427.10, 427.11, 427.19, 428.99, 782.49	I50, I11.0, I13.0, I13.2
Peripheral vascular disease	1	440–445	I70–I74, I77
Cerebrovascular disease	1	430–438	I60–I69, G45, G46
Dementia	1	290.09–290.19, 293.09	F00–F03, F05.1, G30
Chronic pulmonary disease	1	490–493, 515–518	J40–J47, J60–J67, J68.4, J70.1, J70.3, J84.1, J92.0, J96.1, J98.2, J98.3
Connective tissue disease	1	712, 716, 734, 446, I35.99	M05, M06, M08, M09, M30–M36, D86
Ulcer disease	1	530.91, 530.98, 531–534	K22.1, K25–K28
Mild liver disease	1	571, 573.01, 573.04	B18, K70.0–K70.3, K70.9, K71, K73, K74, K76.0
Diabetes I and II	1	249.00, 249.06, 249.07, 249.09, 250.00, 250.06, 250.07, 250.09	E10.0, E10.1, E10.9, E11.0, E11.1, E11.9
Hemiplegia	2	334	G81, G82
Moderate to severe kidney disease	2	403, 404, 580–584, 590.09, 593.19, 753.10–753.19, 792	I12, I13, N00–N05, N07, N11, N14, N17–N19, Q61
Diabetes with end organ damage	2	249.01–249.05, 249.08, 250.01–250.05, 250.08	E10.2–E10.8, E11.2–E11.8
Any tumor	2	140–194	C00–C75
Leukemia	2	204–207	C91–C95
Lymphoma	2	200–203, 275.59	C81–C85, C88, C90, C96
Moderate to severe liver disease	3	070.00, 070.02, 070.04, 070.06, 070.08, 573.00, 456.00–456.09	B15.0, B16.0, B16.2, B19.0, K70.4, K72, K76.6, I85
Metastatic solid tumor	6	195–199	C76–C80
AIDS	6	079.83	B21–B24

Table S2 Diagnosis codes for myocardial infarction according to the International Classification of Diseases, 8th (ICD-8) and 10th (ICD-10) revision

Myocardial infarction	ICD-8 codes	ICD-10 codes
Prior to the scan	410	I21, I22, I23
Outcome	410	I21

Table S3 Risk and hazard ratio of MI and all-cause death within 5 years following a normal versus abnormal scan

Outcome	Scan result	No. of events	Risk % (95% CI)	Risk difference % (95% CI)	Hazard ratio (95% CI)	
					Unadjusted	Adjusted*
MI	Normal	22	11.4 (7.2 – 16.7)	8.1 (1.9 – 14.2)	1 (reference)	1 (reference)
	Abnormal	85	19.4 (15.9 – 23.3)		1.64 (1.03 – 2.62)	1.53 (0.95 – 2.47)
All-cause death	Normal	14	7.9 (4.7 – 13.0)	3.9 (–1.1 – 8.9)	1 (reference)	1 (reference)
	Abnormal	50	11.8 (9.1 – 15.3)		1.48 (0.82 – 2.67)	1.19 (0.65 – 2.17)

Note: Included are patients with a first-time MI 0–1 year before the scan. *Adjusted for sex, age, and comorbidity level.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

Table S4 Risk and hazard ratio of MI and all-cause death within 5 years following a normal versus abnormal scan.

Outcome	Scan result	No. of events	Risk % (95% CI)	Risk difference % (95% CI)	Hazard ratio (95% CI)	
					Unadjusted	Adjusted*
MI	Normal	19	11.4 (6.8 – 17.2)	5.6 (–1.1 – 12.3)	1 (reference)	1 (reference)
	Abnormal	64	17.0 (13.4 – 21.0)		1.62 (0.97 – 2.70)	1.57 (0.93 – 2.65)
All-cause death	Normal	13	8.2 (4.8 – 13.7)	6.6 (0.9 – 12.2)	1 (reference)	1 (reference)
	Abnormal	54	14.8 (11.5 – 18.8)		1.88 (1.03 – 3.45)	1.56 (0.84 – 2.89)

Note: Included are patients with a first-time MI >1–5 years before the scan. *Adjusted for sex, age, and comorbidity level.

Abbreviations: CI, confidence interval; MI, myocardial infarction.

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