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Mismatch of presenting symptoms at first and recurrent acute myocardial infarction. From the MONICA/KORA Myocardial Infarction Registry

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Abstract

Background: It is unknown whether the symptoms of first and recurrent acute myocardial infarction (AMI) are similar in the same person. This study examined the frequency of symptom mismatch, which factors are associated with a symptom mismatch and how symptom mismatch is related to 28-day case fatality.

Design: Observational study.

Methods: The sample consisted of 1282 persons with a first and recurrent AMI, recruited from a population-based AMI registry, 1985–2011. Occurrence of 11 symptoms was recorded in first and recurrent AMI using standardized patient interview. Logistic regression modelling adjusted for demographic and clinical variables was applied.

Results: Mismatch was highest for dyspnoea (40.6%) and lowest for chest symptoms (10.4%). Compared with women, men were less likely to have a mismatch of pain between the shoulder blades (odds ratio (OR) 0.58, 95% confidence interval (CI) 0.43–0.79), pain in the throat/jaw (OR 0.67, 95% CI 0.50–0.91), nausea (OR 0.62, 95% CI 0.47–0.82), vomiting (OR 0.50, 95% CI 0.36–0.71), or fear of death (OR 0.71, 95% CI 0.53–0.94), or to have three or more mismatching symptoms (OR 0.60, 95% CI 0.45–0.79). Persons with diabetes were more likely to have a mismatch in chest symptoms, whereas persons with hyperlipidaemia or persons who received any revascularization therapy at first infarction were significantly less likely to have a mismatch of chest symptoms. Twenty-eight-day case fatality significantly increased with the number of mismatching symptoms (OR 1.14, 95% CI 1.02–1.28).

Conclusions: Patients with AMI may benefit from information about the possibility that a recurrent infarction may be associated with different symptoms.

Keywords

Myocardial infarction, re-infarction, symptoms, survival

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Introduction

An acute myocardial infarction (AMI) is commonly associated with a wide range of possible symptoms, including chest discomfort (e.g. pain, pressure, or squeezing) that can radiate to the arms, back, neck, jaw, or stomach, shortness of breath, sweating, and nausea.[1] A good knowledge of common AMI symptoms is a prerequisite for seeking immediate care. Studies have demonstrated that symptom-related factors are important reasons for pre-hospital delay.[2,3] Since an immediate start of treatment is positively

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related to AMI outcomes, it is not surprising that symptoms were also found to be associated with short-term case fatality and even long-term mortality.[4–5]

The range and nature of AMI symptoms can vary according to the demographic and clinical characteristics of the affected person. Differences in symptoms, specifically in the occurrence of the most typical chest pain, were found for gender, for type of AMI, for persons with and without diabetes, and for different age groups.[4,6–10] However, it is not clear so far whether the symptoms of a re-infarction are similar to the symptoms of the first infarction. In the qualitative study of Pattenden et al.,[11] who interviewed 22 patients with re-infarction, 91% of the patients reported that the symptoms of the re-infarction were not similar to those of the first infarction. Several participants mentioned that this negatively affected their decision to seek help.

However, there is a lack of studies that provide a more comprehensive analysis and quantification of the mismatch of first and re-infarction symptoms in a larger population of AMI patients and that identify factors contributing to symptom mismatch. No previous study has compared first and recurrent AMI symptoms in the same patients. The relation between symptom mismatch and case fatality is unknown.

Thus, the objective of this study was to examine how often mismatch of first and recurrent AMI symptoms occurs in a population-based sample of patients with recurrent infarction, and which patient characteristics are associated with a symptom mismatch. In addition, the study was able to investigate the association between 28-day case fatality and symptom mismatch.

Methods

This study uses data from the population-based Augsburg Coronary Event Registry, which was implemented in 1984 as part of the WHO-MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) project. After the termination of MONICA in 1995, the registry became part of the framework of KORA (Cooperative Health Research in the Region of Augsburg). Since 1984, all cases of coronary deaths and non-fatal AMI of the 25–74-year-old study population in the city of Augsburg and the two adjacent counties (about 600,000 inhabitants) have been continuously registered. Methods of case finding, diagnostic classification of events, and data quality control have been described elsewhere.[12,13]

Sample

This study is based on a subsample of all registered cases ($n = 15{,}606$) with an incident AMI between 1 January 1985 and 31 December 2011 who survived longer than 24 hours. In the present analysis, 1287 patients who had both a first and a recurrent AMI during this time period were included. Five patients were excluded since information on all 11 AMI symptoms was missing for first or recurrent AMI. Finally, the present analyses comprised 1282 persons (990 males and 292 females) with recurrent infarction aged 25 to 74 years at the time of AMI.

Data collection

Patients were interviewed by trained study nurses during their hospital stays (first and re-infarction) using a standardized questionnaire after they had been transferred from the intensive care unit. The interviews included demographic data, data on cardiovascular risk factors, medical history, co-morbidities, and symptoms associated with the AMI event. The initial question on AMI symptoms was related to the presence of chest pain or feelings of pressure or tightness. Subsequently, the patients were asked whether they had experienced any other symptoms and complaints. If they agreed, they were queried on the occurrence of ten additional symptoms: pain in the left shoulder/arm/hand, pain in the right shoulder/arm/hand, pain in the throat/jaw, pain between the shoulder blades, pain in the upper abdomen, nausea, vomiting, diaphoresis, dyspnoea, and fear of death.

The patients were asked whether they were married (yes/no), whether they currently lived alone (yes/no), whether they had ever smoked or had stopped smoking (current smoker/ex-smoker/never smoked), and whether they had been diagnosed as having high blood pressure, high blood lipids, or blood glucose prior to the AMI event. Self-reported history of angina pectoris, hypertension, hyperlipidaemia, or diabetes (yes/no) was only considered if the chart review confirmed these diseases. The history of stroke (yes/no) was only determined by self-report. Moreover, patients were asked about their nationality and whether both parents were German. If the patient or either parent did not have German nationality, a migration background (yes/no) was noted. Education was dichotomized into low-level (9 years of school education) and higher-level school education (more than 9 years). Body mass index (BMI) was determined by assessment of height and weight during the hospital stay. Obesity (yes/no) was defined as $BMI > 30\,kg/m^2$. Patients were asked for the exact time of symptom onset and arrival at the hospital. Pre-hospital delay time was defined as the time from symptom onset to arrival at the hospital. The patient-reported information on arrival at the hospital was validated using the admission data from the emergency department. Application of any

revascularization therapy (yes/no) was defined as having received thrombolysis, percutaneous coronary intervention, or coronary artery bypass surgery during the hospital stay. Information on AMI type (ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (N-STEMI), bundle branch block) and AMI location (anterior, posterior, undetermined) was documented in the patients' medical records. Severely reduced left ventricular ejection fraction (LVEF) was recorded if echocardiography, ventriculography, or radionuclide ventriculography performed during the hospital stay revealed a LVEF < 30% (yes/no). This information was only collected in patients with AMI later than 1999.

Mortality was ascertained by a regular check of the vital status of all registered persons of the MONICA/KORA MI registry through the population registries. Death certificates were obtained from local health departments.

The study was approved by the Ethics Committee of the Bavarian Medical Association. All participants submitted written informed consent before being enrolled in the study.

Data analysis

The occurrence of each of the 11 symptoms at first and recurrent infarction was cross-tabulated. For each symptom, a mismatch was defined if a symptom occurred at the first AMI but did not reappear at the second AMI, or if a symptom was not present at the first AMI but was reported at the second AMI. A summary variable reflects the number of mismatching symptoms across all 11 symptoms. A score of 0 indicates a complete mismatch of the symptom scope, whereas a score of 11 indicates a perfect symptom match.

The relationship between the mismatch of each of the 11 AMI symptoms and potential associated variables (all variables displayed in Table 1) was examined using multivariate logistic regression modelling with backward variable elimination. A significant ($p < 0.05$) association of an independent variable with any of the 11 dependent variables (symptom mismatch yes/no) in the univariate analysis was used as the criterion for entry in the multivariate model. The models computed for each of the 11 AMI symptoms included sex, age at first infarction, time between first and re-infarction, obesity at re-infarction, hypertension, hyperlipidaemia and diabetes prior to re-infarction, same AMI type (STEMI, N-STEMI, bundle branch block) at first and recurrent infarction (yes/no), and any revascularization treatment at first infarction (yes/no). The final model only includes variables that significantly ($p < 0.05$)

Table 1. Demographic and clinical characteristics of the sample ($n = 1282$). Values n (%) unless otherwise stated.

	First infarction	Re-infarction
Year of AMI		
1985–1994	588 (45.7)	247 (19.3)
1995–2004	524 (40.9)	509 (39.7)
2005–2011	170 (13.3)	526 (41.0)
Male sex	990 (77.2)	
Age (years) (mean (SD))	57.8 (9.48)	63.4 (9.4)
Married	973 (80.5)	
Living alone	152 (12.6)	
School education[a]		
9 years	247 (55.1)	
>9 years	201 (44.9)	
Migration background[a]	115 (15.4)	
Smoking[a]		
Current smoker	555 (45.4)	288 (25.0)
Former smoker	305 (25.0)	520 (45.1)
Never-smoker	362 (29.6)	344 (29.9)
Obesity	221 (17.2)	272 (21.2)
Hypertension[a]	819 (64.1)	1012 (79.1)
Hyperlipidaemia[a]	832 (66.6)	947 (74.4)
Diabetes[a]	364 (28.4)	497 (38.8)
Left ventricular ejection fraction <30%[a]	13 (4.2)	53 (12.2)
AMI type[a]		
STEMI	550 (45.8)	403 (32.9)
NSTEMI	587 (48.9)	704 (57.4)
Bundle branch block	63 (5.3)	119 (9.7)
AMI location		
Anterior	576 (44.9)	451 (35.2)
Posterior	540 (42.1)	476 (37.1)
Undetermined	166 (13.0)	355 (27.7)
Revascularization therapy[a]		
Thrombolysis	358 (32.8)	178 (16.6)
Percutaneous coronary intervention	467 (36.5)	563 (44.1)
Coronary artery bypass graft	93 (7.3)	177 (13.9)
Any reperfusion therapy	785 (61.2)	822 (64.1)
Discharge medication[a]		
Antiplatelet agents	1083 (86.4)	936 (90.0)
Beta blockers	959 (76.6)	875 (84.1)
ACEI/ARB	534 (42.6)	701 (55.9)
Diuretics	492 (39.3)	604 (58.1)
Calcium channel blockers	418 (33.4)	277 (26.7)
Statins	514 (41.1)	685 (65.9)
28-day case fatality	–	117 (9.1)
Pre-hospital delay time (minutes) (Median (25%/75% percentile))	180 (88/673)	148.5 (70/421)

(continued)

Table 1. Continued.

	First infarction	Re-infarction
Time between first and re-infarction (years) (Median (25%/75% percentile))	–	4.1 (1.3/8.7)

ACEI: angiotensin-converting enzyme inhibitors; AMI: acute myocardial infarction; ARB: angiotensin receptor blockers. [a]Percentages refer to non-missing observations.

contribute to the model. Age and sex were forced to stay in the model.

The question whether a mismatch of any of the 11 symptoms or the summary score of mismatching symptoms is associated with 28-day case fatality was also explored by multivariate logistic regression modelling with backward elimination of variables. Regression models were calculated for each of the 11 symptoms and the summary score of mismatching symptoms. First, the association between the single symptom mismatch and 28-day case fatality adjusted for age and sex was calculated. Since we aimed at assessing the specific effects of symptom mismatch on case fatality irrespective of the effect of specific symptoms at re-infarction, we included the respective symptom at re-infarction in the second model (e.g. regression model for mismatch of vomiting was adjusted for presence of vomiting at re-infarction). Finally, a parsimonious model was built by backward selection. Additional variables that are known from literature to be associated with survival in AMI patients were included as potential confounders: sex; age at re-infarction; year of re-infarction; time between first and re-infarction; history of stroke, diabetes, hypertension, or hyperlipidaemia; smoking status; obesity at re-infarction; pre-hospital delay time; AMI type; and any revascularization treatment at re-infarction. This model only includes variables that significantly ($p < 0.05$) contribute to the model. The respective symptom mismatch, the symptom at re-infarction, and age and sex were forced to stay in the model. The regression model for the summary score of mismatching symptoms was calculated accordingly, with adjustment for age and sex in the first step, inclusion of all 11 symptoms at re-infarction in the second step, and the above-named confounders in the parsimonious model. Multicollinearity among the independent variables was examined by assessing Variance Inflation Factors (VIF) in the full models.[14]

Since information on LVEF was only available for patients with re-infarction after 1999, a sensitivity analysis was performed by including dummy coded variables into the models (LVEF $< 30\%$, $\geq 30\%$, missing information).

All full logistic regression models were tested for an interaction effect of age and sex and for interactions between the respective symptom mismatch and age, sex, diabetes, hypertension, hyperlipidaemia, any revascularization treatment, or time between first and re-infarction.

Results

The sample consisted of 1282 patients (77.2% men) with a mean age of 57.8 years at first and 63.4 years at second infarction, respectively. Further characteristics of the sample are displayed in Table 1.

Among all patients, 94.3% (95.5% among women, 93.9% among men) had a different scope of symptoms at re-infarction compared with first infarction. On average, the patients had 3.2 ± 1.9 mismatching symptoms. The lowest percentage of mismatch was found for chest symptoms (10.4%), whereas other symptoms showed a mismatch rate ranging between 15.5% (pain in the upper abdomen) and 40.6% (dyspnoea) (see Table 2).

Multivariate logistic regression analysis revealed that men were less likely to have a mismatch of pain between the shoulder blades, pain in the throat/jaw, nausea, vomiting, and fear of death compared with women. In addition, the number of mismatching symptoms was significantly lower in men than in women (see Table 3). In contrast, different factors emerged which that were significantly related to chest symptoms. Persons with diabetes were more likely to have a mismatch, whereas persons with hyperlipidaemia or persons who had received any revascularization therapy at first infarction were significantly less likely to have a mismatch of chest symptoms.

The bivariate analyses of the association between symptom mismatch and 28-day case- fatality showed that the number of deaths was significantly higher ($p < 0.01$) among persons with a mismatch of chest symptoms (20.5%) compared with persons with matching symptoms (7.3%). Patients who reported chest pain at first AMI but had no chest pain at recurrent infarction showed an increased risk (27.8% deaths) compared with those who had chest pain at both AMIs (7.0%) and those who did not have chest pain at first AMI, but had chest pain at recurrent AMI (4.8%). However, patients without chest pain at both events had a slightly higher risk (33.3%). In addition, a mismatch of dyspnoea was associated with a significantly ($p < 0.041$) higher number of deaths (11.0% vs. 7.7%). After adjustment for the presence of symptoms at re-infarction and for other relevant covariables in the multivariate logistic regression analysis, a mismatch in any of the single symptoms a

Table 2. Frequency and mismatch of presenting symptoms at first and recurrent infarction.

Symptom	*n*	First infarction *n* (%)	Re-infarction *n* (%)	Mismatch *n* (%)	No longer present at re-infarction *n* (%)[a]	New at re-infarction *n* (%)[b]
Chest pain or feelings of pressure or tightness	1265	1208 (95.5)	1160 (91.7)	132 (10.4)	90 (68.2)	42 (31.8)
Pain left hand/arm/shoulder	1267	693 (54.7)	595 (47.0)	438 (34.6)	268 (61.2)	170 (38.2)
Pain right hand/arm/shoulder	1261	375 (29.7)	314 (24.9)	351 (27.8)	206 (58.7)	145 (41.3)
Pain between shoulder blades	1259	309 (24.5)	269 (21.4)	322 (25.6)	181 (56.2)	141 (43.8)
Pain throat/jaw	1258	358 (28.5)	309 (24.6)	367 (29.2)	208 (56.7)	159 (43.3)
Pain upper abdomen	1258	128 (10.7)	111 (8.8)	195 (15.5)	106 (54.4)	89 (45.6)
Diaphoresis	1266	662 (52.3)	544 (43.0)	508 (40.1)	313 (61.6)	195 (38.4)
Dyspnoea	1272	573 (45.1)	588 (46.2)	517 (40.6)	251 (48.5)	266 (51.5)
Nausea	1270	431 (33.9)	329 (25.9)	460 (36.2)	281 (61.1)	179 (38.9)
Vomiting	1267	171 (13.5)	101 (8.0)	190 (15.0)	130 (68.4)	60 (31.6)
Fear of death	1260	373 (29.6)	288 (22.9)	399 (31.7)	242 (60.7)	157 (38.3)

[a]Symptom present at first and re-infarction or absent at first and re-infarction. [b]Percentages refer to persons with symptom mismatch.

Table 3. Significant ($p < 0.05$) predictors of mismatch of the presenting symptoms and the number of mismatching symptoms. Multivariable logistic regression models adjusted for age and sex. Analysis of 'pain in the left shoulder/arm/hand', 'pain in upper abdomen', and 'diaphoresis' revealed no significant predictors.

Symptom	OR (95% CI)	*p*
Chest pain or feelings of pressure or tightness		
Diabetes	1.63 (1.12–2.36)	0.009
Hyperlipidaemia	0.58 (0.39–0.85)	0.005
Reperfusion therapy	0.58 (0.40–0.84)	0.006
Pain right shoulder/arm/hand		
Match regarding infarction type	1.35 (1.05–1.73)	0.020
Time between first and re-infarction (per year)	1.03 (1.01–1.06)	0.013
Pain between shoulder blades		
Men	0.58 (0.43–0.79)	<0.001
Pain throat/jaw		
Men	0.67 (0.50–0.91)	0.023
Age	0.98 (0.97–0.99)	0.025
Dyspnoea		
Hypertension	1.42 (1.07–1.89)	0.015
Nausea		
Men	0.62 (0.47–0.82)	<0.001
Hypertension	0.71 (0.54–0.94)	0.018
Vomiting		
Men	0.50 (0.36–0.71)	<0.001
Fear of death		
Men	0.71 (0.53–0.94)	0.018
≥3 mismatching symptoms		
Men	0.60 (0.45–0.79)	<0.001
Time between first and re-infarction (per year)	1.04 (1.01–1.06)	0.002

mismatch remained to be significantly associated with a higher risk to die (see Table 4). However, the number of experienced mismatching symptoms was significantly associated with an increased risk to die within 28 days. For each additional mismatching symptom, the odds to die increased by 14% (OR 1.14, 95% CI 1.02–1.28, $p = 0.026$). The parsimonious regression models shown in Table 4 also revealed that persons who presented with chest symptoms at re-infarction had a significantly lower odds to die (OR 0.26, 95% CI 0.10–0.65, $p = 0.004$). Reduced case- fatality was also found for patients with pain in the left upper extremity (OR 0.43, 95% CI 0.26–0.71, $p < 0.001$), pain between the shoulder blades (OR 0.33, 95% CI 0.13–0.79, $p = 0.013$), vomiting (OR 0.34, 95% CI 0.12–0.96, $p = 0.043$), diaphoresis (OR 0.48, 95% CI 0.29–0.82, $p = 0.007$), and fear of death (OR 0.08, 95% CI 0.02–0.34, $p < 0.001$).

A sensitivity analysis including LVEF did not considerably affect the results. In all logistic regression analyses no significant interaction effects were found. VIFs were below 2.5, indicating no relevant multicollinearity among the covariables.[14]

Discussion

The present study demonstrated that the most common AMI symptom, chest pain, was least likely to change from first to recurrent AMI, with only 10.4% of persons showing a mismatch of chest symptoms. Mismatch in other single symptoms was more likely, ranging from 15.5% (pain in the upper abdomen) to 40.6% (dyspnoea). However, since patients commonly do not present with only one single symptom, but four

Table 4. Associations between symptom mismatch and 28-day case fatality. Results of multivariate logistic regression analyses.

Symptom	OR (95% CI)	*p*–value
Chest pain or feelings of pressure or tightness		
Adjusted for sex and age	3.35 (2.05–5.45)	<.001
+adjusted for symptom at re-infarction	0.82 (0.34–1.97)	0.660
Parsimonious model[a]	0.88 (0.35–2.22)	0.777
Pain left shoulder/arm/hand		
Adjusted for sex and age	0.90 (0.59–1.37)	0.613
+adjusted for symptom at re-infarction	0.81 (0.53–1.24)	0.321
Parsimonious model[a]	0.86 (0.54–1.36)	0.507
Pain right shoulder/arm/hand		
Adjusted for sex and age	1.04 (0.67–1.62)	0.851
+adjusted for symptom at re-infarction	1.39 (0.89–2.19)	0.152
Parsimonious model[a]	1.27 (0.77–2.10)	0.347
Pain between shoulder blades		
Adjusted for sex and age	0.76 (0.47–1.24)	0.275
+adjusted for symptom at re-infarction	1.03 (0.62–1.70)	0.922
Parsimonious model[a]	1.01 (0.58–1.76)	0.965
Pain throat/jaw		
Adjusted for sex and age	0.92 (0.59–1.44)	0.704
+adjusted for symptom at re-infarction	1.13 (0.71–1.79)	0.607
Parsimonious model[a]	1.08 (0.65–1.79)	0.771
Pain upper abdomen		
Adjusted for sex and age	0.78 (0.42–1.42)	0.414
+adjusted for symptom at re-infarction	0.71 (0.34–1.46)	0.348
Parsimonious model[a]	0.71 (0.31–1.65)	0.426
Diaphoresis		
Adjusted for sex and age	1.29 (0.87–1.93)	0.257
+adjusted for symptom at re-infarction	1.21 (0.81–1.81)	0.362
Parsimonious model[a]	1.24 (0.79–1.93)	0.350
Dyspnoea		
Adjusted for sex and age	1.47 (0.99–2.17)	0.056
+adjusted for symptom at re-infarction	1.47 (0.99–2.18)	0.056
Parsimonious model[a]	1.31 (0.85–2.03)	0.226
Nausea		
Adjusted for sex and age	1.16 (0.77–1.74)	0.491
+adjusted for symptom at re-infarction	1.28 (0.84–1.95)	0.246
Parsimonious model[a]	1.50 (0.94–2.39)	0.091
Vomiting		
Adjusted for sex and age	1.21 (0.70–2.07)	0.498
+adjusted for symptom at re-infarction	1.43 (0.81–2.52)	0.216
Parsimonious model[a]	1.90 (1.02–3.52)	0.052
Fear of death		
Adjusted for sex and age	0.80 (0.51–1.24)	0.315
+adjusted for symptom at re-infarction	1.12 (0.71–1.77)	0.636
Parsimonious model[a]	1.14 (0.68–1.89)	0.627
Number of mismatching symptoms		
Adjusted for sex and age	1.16 (1.05–1.28)	0.003
+adjusted for symptoms at re-infarction	1.14 (1.02–1.27)	0.020
Parsimonious model[a]	1.14 (1.02–1.28)	0.026

[a]Covariables were: symptom at re-infarction; sex; age at re-infarction; year of re-infarction; time between first and re-infarction; history of stroke, diabetes, hypertension, or hyperlipidaemia; smoking status; obesity at re-infarction; pre-hospital delay time; AMI type; and any reperfusion treatment at re-infarction.

symptoms on average, the mismatch regarding the whole spectrum of symptoms adds further important information. Our finding that 94.3% of patients had a different set of symptoms at re-infarction is comparable to the small qualitative study of Pattenden et al.,[11] in which 91% of the 22 patients reported a symptom mismatch.

The finding that women are more likely to have a mismatch of single symptoms that are less typical for AMI, such as nausea, vomiting, and pain in the throat/jaw, correlates with studies demonstrating that women experience a wider range of unspecific symptoms compared with men.[6,15–17]

Diabetes, hyperlipidaemia and revascularization therapy of first AMI emerged as significant predictors of mismatch in chest symptoms. Diabetes has already been identified as a predictor of the absence of chest pain in patients with AMI.[9,10,18] We hypothesize that any neural impairment due to diabetes may have increased from first to recurrent infarction and culminated in a non-perception of chest pain at re-infarction. This mechanism is supported by the finding that most of the persons (68.2%) who had a mismatch of chest symptoms experienced no chest symptoms at re-infarction. The role of hyperlipidaemia and previous revascularization therapy, however, has not yet been sufficiently described in this context. Culić et al.[18] found that hyperlipidaemia was not associated with absence of chest pain in 1996 patients with first AMI, whereas Canto et al.[10] demonstrated in more than 1,000,000 patients with first or recurrent AMI that hyperlipidaemia, prior percutaneous coronary intervention, and prior coronary artery bypass grafting were related to a higher likelihood of having chest pain.

However, unlike our work, neither of these studies compared first and recurrent AMI symptoms in the same patients.

Our results clearly demonstrate that the presence of a number of AMI symptoms (chest symptoms, pain in the upper left extremity, pain between shoulder blades, vomiting, diaphoresis, and fear of death) at re-infarction significantly reduces 28-day case fatality. The results regarding diaphoresis and fear of death are consistent with our previous study, which was limited to patients with first AMI.[5] The presence or absence of certain single symptoms seems to be more important for the prediction of 28-day case fatality than the mismatch of single symptoms. Nevertheless, a higher number of mismatching symptoms was found to be associated with an increased risk of death within 28 days after AMI after adjustment for relevant confounders. The causes of an increased mortality in patients without typical symptoms or with a high number of mismatching symptoms may be twofold: (a) recognition of symptoms as well as in-hospital diagnosis and (b) treatment may be delayed in these persons.

To our knowledge, this is the first study to explore symptom match in the same patients with first and recurrent AMI based on a population-based sample. The strengths of this study are the large sample of patients consecutively hospitalized with validated first and second AMI, the inclusion of patients in a defined area and according to defined criteria, the comprehensive collection of data on socio-demographic characteristics, risk factors, prior diseases, and in-hospital treatment, and the standardized patient-reported assessment of symptoms soon after the AMI over 26 years.

Limitations of the study include the restriction to patients younger than 75 years at the AMI. Patients who died within 24 hours after admission or before the interview could not be included. Patients who had a STEMI at both first and re-infarction may have been more likely to be excluded for this reason than patients with N-STEMI. Since STEMI and N-STEMI patients differ regarding symptoms at presentation,[8] this selection might have influenced the results. Between 1985 and 2011, definition and treatment of AMI changed considerably,[19] and we cannot exclude the possibility that these circumstances have affected the results of our study in any way, despite the adjustment for the event year in the statistical analyses. The assessment of symptoms did not include information about the severity and quality of symptoms and the distress associated with them, or the chief symptom if more than one symptom occurred. History of stroke was only self-reported by the patients. Further, we were not able to consider some other relevant determinants of post-AMI survival, such as renal dysfunction, severe comorbidities (e.g. cancer), and location and number of affected vessels. Thus, residual confounding cannot be completely excluded. Since we performed a great number of statistical comparisons, we cannot exclude the possibility that the significant findings may also be the result of type I error associated with multiple testing.

Finally, the study was performed in Germany, and it is unknown whether the findings are generalizable to other countries.

Our findings have relevant implications for the education of patients with first AMI. Since mismatch of symptoms is most common, patients – specifically women, persons with diabetes, and persons without hyperlipidaemia or revascularization treatment – may benefit from information about the possibility that a recurrent infarction may be associated with different symptoms. It appears particularly important to increase patients' awareness of the possibility that known symptoms will not be present at the recurrent infarction, because absence of typical AMI symptoms is associated with an increased 28-day case fatality. Further research is needed in order to confirm or refute the results of the present study.

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Conflict of interest

None declared.

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