

ORIGINAL ARTICLE

Mortality Following Myocardial Infarction in Women and Men

An Analysis of Insurance Claims Data from Inpatient Hospitalizations

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SUMMARY

Introduction: The results of previous studies of the association between gender and mortality following hospital admission due to acute myocardial infarction are inconsistent. National data for Germany have been lacking to date. Hence the objective of this study was to analyze this association on the basis of a nationwide dataset.

Methods: The analysis was carried out using insurance claims data from inpatients insured by the statutory health insurer AOK, whose main diagnosis was acute myocardial infarction and who were discharged from hospital in the years 2004 and 2005. Several mortality endpoints were used, including 30-day mortality and one-year mortality.

Results: 132 774 male and female patients were included. Crude analyses showed a pronounced excess mortality in women (odds ratio 30-day mortality = 1.65; 95% confidence interval = 1.59 to 1.70). However, after adjustment for age (in deciles) practically equal mortality was observed for female and male patients (odds ratio 30-day mortality = 1.00; 95% confidence interval = 0.96 to 1.03). Only in the comparatively small group of male and female patients up to the age of 50 was a slightly increased mortality observed in women (odds ratio 30-day mortality = 1.09; 95% confidence interval = 0.85 to 1.40).

Discussion: To our knowledge, this study is the first nationwide analysis focusing on the association between gender and survival following hospital admission due to acute myocardial infarction. Different results from earlier regional studies may be explained by selection bias or inadequate risk adjustment.

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Many studies have examined the connection between sex and mortality in patients hospitalized with acute myocardial infarction, but these studies have yielded conflicting results (1–12). Moreover, the small number of studies that have been performed on this subject in Germany to date were based on data from regional or nationwide registries, which do not necessarily reflect the state of care of acute myocardial infarction in all German hospitals in which this condition is treated.

Nor have these German studies yielded uniform results. For example, an analysis of data derived from the Berlin Myocardial Infarction Registry revealed a higher mortality among women with ST-segment elevation myocardial infarction (STEMI) than among men with the same condition (10). For the 76-and-above age group, no excess mortality among women could be found after risk adjustment (9).

Analyses based on the data from the MITRA registry have shown, on the one hand, an elevated in-hospital mortality among women with STEMI, but, on the other hand, comparable long-term survival for men and women after adjustment for age (4). Similar results were obtained regarding patients with STEMI after cardiopulmonary resuscitation in analyses based on the combined MITRA and MIR registries (2). In contrast, an age-adjusted analysis of ACOS registry data on patients with non-ST-segment elevation myocardial infarction (NSTEMI) did not reveal any greater mortality in women than in men (3).

Data from the population-based MONICA/KORA myocardial infarction registry in Augsburg were analyzed to calculate mortality rates for the periods 1985 to 1987 and 2001 to 2003. The raw mortality figures (pre-hospital, first day of hospitalization, and days 2 to 28) were significantly higher for women than for men in the earlier period, but, in the later period, women had an only marginally higher mortality than men, even without adjustment for age (6).

The purpose of the present study is to analyze current nationwide data from Germany on this subject.

Methods

Nationwide billing data from hospitalized patients covered by the statutory health insurance carrier AOK

TABLE 1

Characteristics of the study population: hospitalized AOK patients (2004–2005) with discharge diagnosis "myocardial infarction," stratified by sex

	Women	Men
Number	57 664	75 110
Age		
Mean	76.1 (76.0–76.1)	66.7 (66.6–66.8)
Interquartile boundaries	70 78 84	58 68 76
Main diagnosis (location of infarct): percent and 95% CI		
Acute transmural anterior wall MI, code I210	22.7 (22.4–23.1)	23.1 (22.8–23.4)
Acute transmural posterior wall MI, code I211	18.1 (17.8–18.4)	23.8 (23.5–24.1)
Acute transmural MI at other locations, code I212	4.8 (4.6–5.0)	4.9 (4.7–5.0)
Acute transmural MI at an unspecified location, code I213	4.0 (3.8–4.1)	3.5 (3.31–3.6)
Acute subendocardial MI, code I214	37.1 (36.7–37.5)	33.8 (33.5–34.2)
Acute MI, not otherwise specified, code I219	13.0 (12.8–13.3)	10.6 (10.4–10.8)
Accompanying illnesses		
Diabetes	38.8 (38.4–39.2)	29.5 (29.2–29.9)
Hypertension	68.1 (67.8–68.5)	66.0 (65.7–66.3)
Heart failure	45.0 (44.6–45.4)	35.2 (34.9–35.6)
Renal failure	22.1 (21.7–22.4)	19.4 (19.1–19.7)
Inpatient procedures/operations		
Diagnostic left heart catheterization*	16.3 (16.1–16.7)	18.3 (18.1–18.6)
Therapeutic left heart catheterization without stent*	3.7 (3.5–3.8)	5.3 (5.1–5.5)
Therapeutic left heart catheterization with stent*	31.7 (31.3–32.1)	49.6 (49.3–50.0)
Aortocoronary bypass	4.6 (4.5–4.8)	8.1 (7.9–8.3)

*The categorization of left heart catheterizations was hierarchical: when a therapeutic left heart catheterization with stent was coded, further left heart catheterizations for the same patient that were either diagnostic or without stent were not coded. Similarly, when a therapeutic left heart catheterization without stent was coded, further diagnostic left heart catheterizations for the same patient were not coded.
MI = myocardial infarction, CI = confidence interval

were obtained according to §301 of the German Social Insurance Law (Sozialgesetzbuch V) and analyzed for the purposes of this study. All hospitalized persons were included who

- were given the main diagnosis of a myocardial infarction (ICD-10 code I21),
- were over 30 years old, and
- were discharged from a hospital in 2004 or 2005.

Follow-up information on survival and insurance status were obtained by consulting AOK membership files.

Cases were dealt with anonymously, and it was possible to analyze not only in-hospital data but also the outcome of each individual case outside the hospital.

Patients who had earlier been acutely hospitalized (in or after the year 2002) with a myocardial infarction coded as their main diagnosis or as a secondary diagnosis were excluded from the analysis. In order to assess the effect of inter-hospital transfers, account was taken of sequential hospitalizations in which the patient was admitted to a second hospital on the same day as, or one day after, discharge from the first hospital (the legal definition of an inter-hospital transfer).

The endpoints that were analyzed were death during the index hospitalization and mortality at 30 days, 90 days, and one year. Patients who were no longer insured by AOK by the end of a given follow-up period were no longer considered in the analysis. This resulted in different numbers of cases being analyzed for the different endpoints. Survival analyses were not calculated, because information was obtained only at fixed follow-up intervals (30 and 90 days and one year). Risk-adjusted analyses were carried out with robust logistic regression with the use of sandwich variance estimators in the STATA 8.2 program package (13, 14).

Results

The characteristics of the patients are listed in *table 1*. The database contains information on 57 664 women and 75 110 men. Women suffering from myocardial infarction were older than their male counterparts by an average of more than nine years (mean) or ten years (median). Women also more commonly had other accompanying illnesses: in particular, the prevalence of diabetes (38.8% vs. 29.5%) and heart failure (45.0% vs.

35.2%) was significantly higher in women than in men. On the other hand, women underwent coronary interventions and procedures less often than men did: for example, the figures for therapeutic cardiac catheterization with stenting were 31.7% for women vs. 49.6% for men, while those for aortocoronary bypass were 4.6% for women vs. 8.1% for men.

Table 1 also lists the sex-specific distribution of patients according to their main diagnosis as a four-position ICD-10 code. Women were found to have a relatively lower frequency of transmural posterior wall infarction than men (18.1% vs. 23.8%), and also a slightly lower frequency of transmural anterior wall infarction (22.7% vs. 23.1%). On the other hand, women were relatively more likely to sustain an acute subendocardial myocardial infarction (37.1% vs. 33.8%) or a myocardial infarction of an otherwise unspecified type (13.0% vs. 10.6%).

The number of patients included in the study, the number of patients that died, and the resulting raw mortality rates are shown in table 2. This table also indicates the raw and age-adjusted odds ratios (OR) for mortality in women versus men at each of the time points for which mortality data were collected.

Raw analysis seemed to indicate a markedly higher mortality for women (e.g., an odds ratio of 1.65 for 30-day mortality, with a 95% confidence interval [CI] of 1.59 to 1.70). After age-adjustment (by deciles), however, the mortality of women and men was seen to be nearly identical (e.g., an odds ratio of 1.00 for 30-day mortality, with a 95% CI of 0.96 to 1.03).

The age-adjusted probability of survival for the entire patient group after one year of follow-up was found to be somewhat higher in women: here, the odds ratio for mortality at one year was 0.93, with a 95% CI of 0.91 to 0.96.

To examine the connection between types of acute myocardial infarction and sex-specific mortality more closely, we determined the association of sex with 30-day mortality, after age adjustment, in each of the myocardial infarction subgroups defined by four-position ICD-10 codes (figure 1). Women were found to have a higher mortality from transmural posterior wall infarction (I211: OR 1.15, 95% CI 1.07 to 1.25) as well as a mildly, but not significantly, increased mortality from transmural infarction at an otherwise unspecified location (I213: OR 1.08, 95% CI 0.95 to 1.23). On the other hand, women had a lower mortality from subendocardial infarction (I214: OR 0.91, 95% CI 0.85 to 0.97) and from otherwise unspecified types of myocardial infarction (I219: OR 0.92, 95% CI 0.85 to 0.99).

An age-adjusted analysis of different age groups defined by different threshold values is shown in figure 2. Only in the relatively small group of patients under age 50 (n = 10 311, 30-day follow-up) did women tend to have a higher mortality in the time period under study (e.g., OR for 30-day mortality: 1.09, 95% CI 0.85 to 1.40); at one year, the higher mortality among women in this age group was statistically significant (OR for one-year mortality: 1.34, 95% CI 1.10 to 1.63; see also table 2).

TABLE 2

In-hospital mortality, 90-day mortality, and one-year mortality by sex in hospitalized AOK patients (2004-2005)

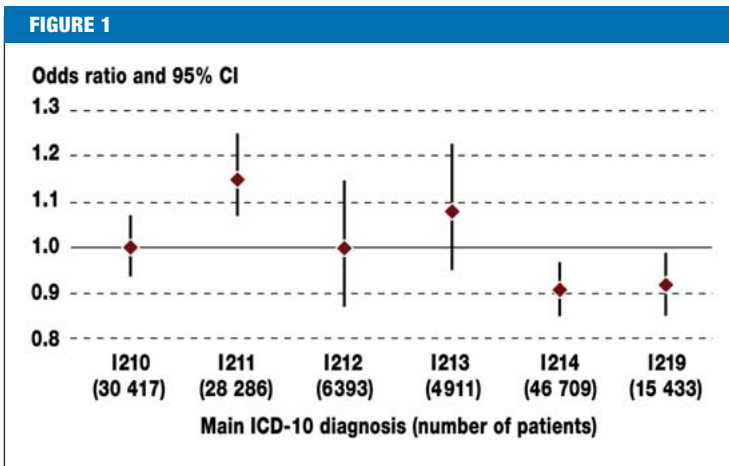
	In-hospital mortality	30-day mortality* ¹	90-day mortality* ¹	One-year mortality* ¹
All patients				
Number	132 774	132 516	132 328	130 161
Percentage of women	43.4 %	43.4 %	43.5 %	43.4 %
Died	18 517	22 135	27 487	36 611
Mortality in percent	13.9 %	16.7 %	20.8 %	28.1 %
Raw odds ratio (95% CI)	1.68 (1.63-1.74)	1.65 (1.59-1.70)	1.69 (1.64-1.74)	1.73 (1.68-1.77)
Age-adjusted odds ratio* ² (95% CI)	1.01 (0.98-1.05)	1.00 (0.96-1.03)	0.99 (0.95-1.02)	0.93 (0.91-0.96)
Patients under age 50				
Number	10 382	10 311	10 278	10 019
Percentage of women	17.7 %	17.7 %	17.7 %	17.7 %
Died	339	433	484	603
Mortality in percent	3.3 %	4.2 %	4.7 %	6.0 %
Age-adjusted odds ratio* ³ (95% CI)	1.15 (0.88-1.51)	1.09 (0.85-1.40)	1.10 (0.87-1.38)	1.34 (1.10-1.63)

*¹ Patients whose insurance status was unclear at the end of follow-up were excluded.

*² Age stratified by deciles

*³ Age in years

Men were taken as the reference population for statistical purposes, i.e., an odds ratio greater than 1 indicates a higher mortality among women, an odds ratio of 1 indicates equal mortality among men and women, and an odds ratio less than 1 indicates a lower mortality among women.



The age-adjusted* odds ratio of women versus men for 30-day mortality after acute myocardial infarction for each four-position ICD-10 code, AOK patients, 2004–2005
* adjusted by age in deciles.

Men were taken as the reference population for statistical purposes, i.e., an odds ratio greater than 1 indicates a higher mortality among women, an odds ratio of 1 indicates equal mortality among men and women, and an odds ratio less than 1 indicates a lower mortality among women.

I210: acute transmural anterior wall myocardial infarction, I211: acute transmural posterior wall myocardial infarction, I212: acute transmural myocardial infarction at other locations, I213: acute transmural myocardial infarction at an unspecified location, I214: acute subendocardial myocardial infarction, I219: acute myocardial infarction, not otherwise specified

Discussion

This article is the first nationwide analysis of the connection between sex and survival after hospital admission for myocardial infarction, with complete registration of all AOK-insured cases occurring across Germany during the study period. Unlike previous German studies, this study was based on data derived from hospital bills, whose use for scientific purposes has been rare in Germany until now. We will therefore discuss the positive features and drawbacks of these data and of the analytical techniques that we chose to apply before proceeding to an interpretation of their content. The adopted analyses were chosen based upon our longstanding experience in dealing with secondary data of this type (15).

Data validity and depth (comprehensiveness)

The data employed here were mainly collected for the purpose of obtaining reimbursement for hospitalizations, rather than for epidemiological studies of patient care. They therefore contain less clinically detailed information than a clinical registry would. For example, the modification of the ICD-10 that is currently in use in Germany does not reliably distinguish between an ST-segment elevation myocardial infarction (STEMI) and a non-ST-segment elevation myocardial infarction (NSTEMI). Rather, most NSTEMIs will probably be coded as subendocardial infarctions (ICD-10: I213). A consequence of this is that the types of myocardial infarction that are included in German registries are usually more narrowly defined than in the present study (2–4, 6, 8–10, 16).

On the other hand, hospital bills for inpatient treatment are subjected to thorough checking for validity by the health insurance carriers to which they are submitted, and by the AOK in particular. Furthermore, these data have also been thoroughly checked by the insurance carriers' medical services ever since a DRG (Diagnosis Related Groups) based system was adopted in Germany, and they can thus be assumed to be valid with a relatively high degree of assurance. In addition, only those main diagnoses usually considered to be especially reliable were used as inclusion criteria. It thus seems unlikely that the results have been distorted to any relevant degree by the erroneous coding of diagnoses.

Practically identical results are found when recurrent myocardial infarction (ICD-10 code I22) is considered in the analysis as well (these results are not shown here). This study provides no information on events occurring before hospital admission. The analyses of the MONICA/KORA myocardial infarction registry in Augsburg, which did take the relevant pre-hospital mortality into account, did not show any elevation of mortality among women in 2001 to 2003.

Selective AOK sample

In comparison to other German registries, the patients in this sample were found to have a higher prevalence of accompanying illnesses, a higher rate of intervention, and a higher mortality. This may be due, on the one hand, to differing case definitions, and on the other hand to the fact that the AOK sample was relatively older on average, and also more heavily burdened with accompanying illnesses. A detailed comparison of the AOK data with data from other German and international registries can be found in the final report of the joint project entitled "Quality Assurance of Inpatient Care with Routine Data" (Qualitätssicherung der stationären Versorgung mit Routinedaten) (17). The existing differences between the AOK sample and the registry samples, however, probably had no significant effect on the sex differences that were found in the present study, because this study only compared women in the AOK patient collective with men in the AOK patient collective.

Risk adjustment

This being said, it must be assumed that the AOK patient collective analyzed here is more socially homogeneous than the study populations of the myocardial infarction registries. Therefore, it might be the case, for example, that an incomplete risk adjustment by social class in previous studies led to an overstatement by those studies of the effect of sex on mortality after acute myocardial infarction. A similar mechanism was recently discussed as a possible explanation of divergent study findings on the cardiovascular effects of postmenopausal hormone therapy (18, 19).

In the data analysis presented in this paper, risk adjustment was performed only for age, and not for any other risk factor. It has been reported, however, that women with myocardial infarction have, on average, more comorbidities than men (3, 4, 8, 9, 11), and our

results also show a trend in this direction (table 1). It follows that an analysis that additionally adjusted for comorbidity would be expected to show a lesser degree of excess mortality for women (8).

The possibility cannot be excluded that accompanying illnesses might be sought, discovered, and coded with unequal thoroughness in male and female patients. Thus, one might speculate that relevant risk factors for myocardial infarction would be better documented in men than in women because the treating physicians had a greater expectation of finding these risk factors, or a greater tendency to ascribe pathogenetic significance to them, in male than in female patients. If these differently documented risks were then used as data inputs in a risk-adjusted model, a major distortion of the analysis would likely result (20), because risk adjustment means that interindividual comparisons are made only between persons who (apparently) belong to the same risk category, according to the data that are obtained. In the situation discussed here, a mechanism of this type would tend to lead to an underestimation of women's risk-adjusted mortality. Because we could not rule out the presence of this type of sex-specific reporting bias in our own data (as in many previous studies), we chose not to perform risk adjustment according to accompanying illnesses in the present analysis.

It turns out, however, that the data on which we based this study in fact yield practically identical results if risk adjustment is performed, either for relevant and presumably pre-existing accompanying illnesses (17) or for the four-position ICD-code subgroups for the main diagnosis (these results are not shown here).

We did not perform risk adjustment based on data concerning interventions that were performed during the inpatient hospitalization, because this would have been methodologically unsound (21).

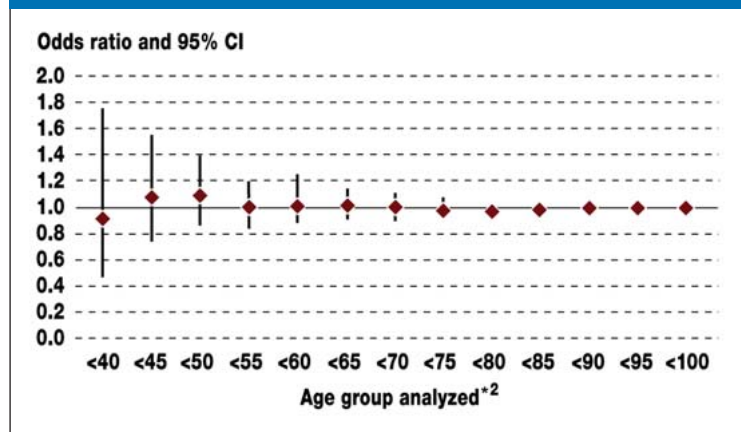
Broader inclusion criteria

The present study employed broader inclusion criteria than the previous German studies. For example, we included not only STEMI and NSTEMI, but also infarctions that might theoretically have occurred as long as 28 days previously. Thus, myocardial infarctions that might not even have been noticed at the time of admission still ended up being included in the analysis. It can also be assumed that some myocardial infarctions that occurred only after the patient was admitted to the hospital were coded with I21 as the main diagnosis on discharge. It is thus no surprise that our database contains data on more patients than the above-mentioned registries (2–4, 6, 8–10, 16).

The potential selectivity of hospital-based registries

The German clinical registries of myocardial infarction mostly depend on the voluntary participation of cooperating hospitals and thus do not necessarily achieve total coverage. For example, selective transfer practices, or selective ambulance transport of patients with myocardial infarction to one hospital or another, might easily distort the results.

FIGURE 2



The age-adjusted^{*1} odds ratio of women versus men in different age groups for 30-day mortality after acute myocardial infarction for each four-position ICD-10 code, AOK patients, 2004–2005

^{*1} adjusted by age in years. Men were taken as the reference population for statistical purposes, i.e., an odds ratio greater than 1 indicates a higher mortality among women, an odds ratio of 1 indicates equal mortality among men and women, and an odds ratio less than 1 indicates a lower mortality among women.

^{*2} Each age group includes the age groups further to the left, e.g., the "<50" age group includes all patients under age 50 and thus contains within it the "<40" age group, etc.

Patient course, follow-up, cost of data collection

Our data analysis in this study took account of intentional or even accidental patient-transfer chains. By addressing the question of mortality at one year, it provided long-term follow-up information derived from a collective of more than 130 000 patients. Such information would presumably be available only to an incomplete extent from the traditional German hospital-based registries, or else it could be obtained only at considerable expense.

Conclusions

Our use of a routinely generated, nationwide database for epidemiological purposes enabled us to address the question of mortality from myocardial infarction with data from a larger number of hospitals than were included in any other study ever performed on this subject in Germany. The inclusion criteria are wider than in the clinical registries, yet they still only cover situations that come under the heading of acute myocardial infarction in general medical parlance. The type of risk adjustment that we performed can be considered robust, i.e., not vulnerable to sex-specific miscoding of comorbidities. Because of the type of risk adjustment that we performed, the data analysis in this study was less likely to miss any truly elevated mortality from myocardial infarction among women than an analysis that additionally adjusted for comorbidities.

From the foregoing critical considerations, the following points emerge:

- After adjustment for age, the sex of the patient was not found to have any influence on the short-term survival rate of persons hospitalized for an acute myocardial infarction of any type (i.e., all types taken together).

- Women were found to have a higher mortality after transmural posterior wall infarction (ICD I211), but a lower mortality for subendocardial infarction (ICD I214) and otherwise unspecified acute myocardial infarction (ICD I219). These results must be viewed with caution, however, because the "remainder categories" (ICD I213 and ICD I219) are both large and non-specific.
- In the overall patient collective, women had a higher one-year survival than men.
- Among patients under 50 years of age, women had a slightly higher mortality than men, particularly after one year of follow-up.

To explain the last finding, one might suppose that myocardial infarction was less commonly diagnosed on presentation among women under 50 than among men under 50, because younger women are not expected to have this condition. The same may well be true of transmural posterior wall infarction: this type of myocardial infarction is frequently associated with less typical, e.g., abdominal, symptoms and with non-diagnostic ECG findings, particularly in cases of arterial occlusion in the circumflex branch distribution.

If this is true, however, the question must still be asked why women were found to have a lower mortality for subendocardial infarction (ICD I214) and otherwise unspecified acute myocardial infarction (ICD I219). A recent, major clinical study provided a critical reassessment of early and aggressive catheterization-based treatment: even though this is currently the standard practice internationally and has been extensively documented, it brings with it additional, prognostically relevant risks including hemorrhage and post-procedural myocardial infarction (22). Perhaps women whose true diagnosis of acute myocardial infarction is initially overlooked might actually benefit from this in some cases, because they are treated conservatively, rather than aggressively (23, 24).

Our analysis of the data does not support the hypothesis that women suffering from acute myocardial infarction in Germany receive poorer in-hospital care than men.

Of course, it could still be the case that, after age adjustment, women and men tend to have myocardial infarctions of differing degrees of severity, as well as accompanying illnesses of differing degrees of severity. It is not possible, however, to solve the problem of differing initial risk for the endpoints under consideration by performing a simple risk adjustment for a few comorbidity variables that are assessed at the time that the infarction takes place (20, 21). The question whether women receive worse care for acute myocardial infarction than men cannot be fully answered by the observational studies that have been carried out to date. Rather, randomized, controlled interventional studies are necessary to answer this and other questions (25). For example, a set of hospitals (or regions) could be selected and randomly divided into two groups ("cluster randomized trial"): in one group, medical personnel would be given specialized training with an emphasis on gender-related aspects of the diagnosis and treatment of myocardial

infarction, while this emphasis would be omitted in the other group. If training of this type indeed has a beneficial effect, then any differences in the outcomes of male and female patients ought to be smaller in the first group.

Conflict of interest statement

The authors declare that they have no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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