Original Research

CARDIOLOGY

Cardiology 2010;116:237–244
DOI: 10.1159/000315451

Received: December 31, 2009
Accepted after revision: May 12, 2010
Published online: August 7, 2010

Are There Options to Prevent Early Occurring Deaths in Acute Myocardial Infarction: Prospective Evaluation of All <24 h In-Hospital Deaths, 2004–2006 – The MONICA/KORA Augsburg Infarction Registry

Bernhard Kuch[b] Wolfgang von Scheidt[b] Birgitt Kling[b] Anja Ehmann[b]
Claudia Greschik[a, c] Christa Meisinger[a, c]

[a]Helmholtz Zentrum München, German Research Center for Environmental Health, Institute of Epidemiology, Neuherberg, [b]1. Medizinische Klinik, Hospital of Augsburg, Teaching Hospital of the Ludwig Maximilians University München, and [c]Hospital of Augsburg, MONICA/KORA Myocardial Infarction Registry, Augsburg, Germany

Key Words
Acute myocardial infarction · Cardiopulmonary resuscitation · Emergency cardiac care · Prevention

Abstract
Objectives: To provide valid clinical data of early in-hospital deaths with presumed acute myocardial infarction (AMI) who are often not included in clinical trials or registries. ***Methods:*** From August 2004 to August 2006 all patients (age 25–84 years) dying within 24 h after hospitalization in a large tertiary care academic teaching hospital were screened regarding an underlying cardiovascular cause of death. ***Results:*** After validation, 79 out of 1,352 patients remained with a final diagnosis of AMI. Sixty-six percent of these experienced prehospital cardiac arrest or shock. In 37% no resuscitation attempts were performed in-hospital, the most common reason being multimorbidity. Only 23% could be transferred to coronary angiography for revascularisation attempts. An independent panel of clinicians judged that only in one patient would another management strategy have been promising. Of interest, 33% of the deceased patients had typical or atypical chest pain the days before the lethal event. ***Conclusion:*** A large percentage of AMI patients who died soon after hospitalization were in critical circulatory state directly before hospitalization. In 37%, in-hospital resuscitation attempts were omitted for understandable reasons. Options for improvement in acute care in the investigated setting were not found. However, in one third of the cases earlier preventive measures might have been reasonable.

Introduction

In-hospital mortality from acute myocardial infarction (AMI) has been shown to have decreased during recent years [1–3]. This was attributed to the timely and intensive adoption of advanced acute care including improved therapeutic strategies as well as improved logistics in seeking patients who might benefit.

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0008–6312/10/1164–0237$26.00/0

Accessible online at:
www.karger.com/crd

Bernhard Kuch, MD
1.Medizinische Klinik, Klinikum Augsburg
Stenglinstrasse 2, DE–86 156 Augsburg (Germany)
Tel. +49 821 400 2956, Fax +49 821 400 3345
E-Mail bernhard.kuch@klinikum-augsburg.de

Most of the data stem from clinical trials performed during different time periods, registries or from administrative data with more or less consecutive and complete patient data acquisition. Thus, similar to the out-of-hospital setting, in many studies and registries the usual lack of availability of valid clinical data in early in-hospital deceased patients may lead to the exclusion of patients who died during the first 24 h after hospitalization [4]. Accordingly, many of the data showing improved in-hospital case fatality may only be able to show the effects of improvements in care for patients who already have survived the critical first hours. This is underscored by the observation of a relatively low in-hospital case fatality in clinical studies or registries [5, 6]. Thus, especially in physician self-reported AMI registries this phenomenon may lead to an under-registration of early occurring AMI-related deaths [7]. Accordingly, it could be shown that around 70% of all 28-day fatal cases occur during the first 24 h using a broader-based epidemiological AMI definition, versus a proportion of only 19% when using a clinical-based definition [4].

Thus, little is known about the magnitude and circumstances of early occurring in-hospital AMI-related deaths. Since this has been claimed to be a prominent 'scientific gap' in our knowledge of potentially AMI-related sudden cardiac death [8], the aims of the present study were to (1) prospectively evaluate whether a presumed in-hospital cardiovascular (CVD)-related death is due to a real AMI in a large tertiary care community-hospital; (2) investigate the characteristics of early deaths, and (3) consider whether early deaths may have been preventable by a different management strategy. The perspective of the study was from the hospital, to evaluate the circumstance of early in-hospital death, but not primarily to follow all patients with survival after out-of-hospital cardiac arrest which requires another strategy. In addition, we compared the prospectively gained data (August 2004 to August 2006) with a representative sample of all early deceased AMI patients in the same hospital over a previous period of 20 years.

Methods

The population-based Augsburg Coronary Event Registry was implemented in October 1984 as part of the World Health Organization's MONICA project (Monitoring Trends and Determinants on Cardiovascular Diseases) [9]. Since 1996 the registry has been carried on within the framework of KORA (Cooperative Health Research in the Region of Augsburg). All cases of fatal coronary events and non-fatal AMIs of the 25- to 74-year-old inhabitants of the city of Augsburg and the two adjacent counties (about 400,000 inhabitants) are continuously registered. Methods of case finding, diagnostic classification of events and data quality control have been described elsewhere [4, 9, 10]. We followed all patients with a suspected diagnosis of AMI who were hospitalized in the study region's major clinic (Klinikum Augsburg, academic teaching hospital of the University of Munich and tertiary care centre offering angiography, PCI, as well as heart surgery facilities on a 24-hour/365-day basis) in which approximately 85% of all AMI cases of the study region are treated. The study was approved by the ethics committee of the Bavarian Medical Association.

For the presently analyzed time period (August 2004 to August 2006) 795 fatal and nonfatal 25- to 75-year-old patients with a validated diagnosis of AMI hospitalized in the Klinikum Augsburg were registered by the MONICA/KORA registry using the usual, previously described screening and validation process [4, 9, 10]. Inclusion of 75- to 84-year-old patients was performed over one year in the same study period and revealed an additional amount of fatal and non-fatal AMI patients of 238 a year (that is around 475 additional elderly AMI cases during the two-year study period).

The present report focuses on all early deceased ($\leq$24 h) patients who died in the Klinikum Augsburg from August 2004 to August 2006. Patients who were referred from other hospitals were not included.

To avoid missing any possible fatal coronary event, in addition to the usual screening process, every patient who died in the Klinikum Augsburg was identified in the pathology book on a daily basis. From all patients dying <24 h after admission, all cases with a potential cardiovascular cause of death were extracted. Comparison of these independently gathered data revealed that most of the possible fatal coronary events identified were also counted by the usual MONICA/KORA screening process (n = 90) by which diagnostic categorization was done retrospectively several weeks after the occurrence of death by gaining postal information from last treating physcians and/or coroners [4]. From these 90 patients, after validation 67 patients remained as definite, probable or possible fatal AMI. An additional number of 12 patients, not classified as cardiovascular death-related by the usual MONICA/KORA screening process, were identified by this prospective approach.

For all these patients, standardized information was sought by a study physician from chart review and interviews from the last treating physicians and/or nurses in the ambulance, the emergency department, the coronary care unit or on the general ward, as well as from family physicians, and coroners or medical examiners and next of kin and other informants. Autopsies were undertaken in two patients only, since autopsy rates in Germany for those who die in old age are traditionally low [4]. In 60% of all early deceased patients an ECG shortly before the occurrence of death was available, in 70% first laboratory results including creatinine-kinase and troponin, and in 90% information regarding the last hours before death were available from chart review and interviews of the last treating physician/ambulance personal, nurses or next of kin.

First Study Objective

To evaluate whether a presumed in-hospital CVD-related death is due to a real AMI, a panel of three physicians reviewed

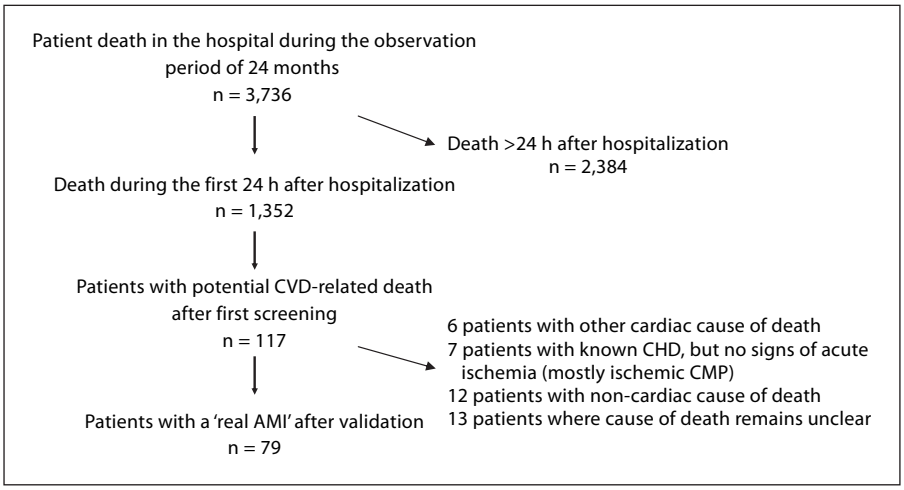

Fig. 1. Identification of time and cause of death occurring in-hospital during the observation period.

each fatal case by using all the above-mentioned information. Disagreements were adjudicated by the committee chairman (B.K.). Classification was performed using the criteria proposed by the Joint Committee of the European Society of Cardiology and American College of Cardiology and other societies and research agencies to improve the consistency of case definitions in epidemiological and clinical studies: 'definite fatal AMI', 'probable fatal AMI' or 'possible fatal coronary event' [11].

Second Study Objective

For all patients classified as having an AMI-related death, the characteristics and circumstances of death were investigated regarding history, place of in-hospital death, and background of CPR measures.

Third Study Objective

In addition, after reviewing the collected data, the panel gave a judgment regarding the appropriateness of the therapeutic strategy. All cases where an initial incorrect diagnosis had been made or an indicated timely invasive strategy would have been promising were considered as being candidates for a different treatment strategy.

Cases in whom at no point in time an appropriate circulation could have been achieved or who have been found dead in bed with no indicated resuscitation (CPR) efforts, as well as those in whom CPR was withheld due to multimorbidity were not considered as candidates for other therapy. Therapeutic hypothermia was not considered as a therapy option because it had not been implemented at the time of this study.

In addition, for comparison with earlier years, data gathered retrospectively were used for investigating the years 1985 until 2004. The data ascertainment and validation processes are described in detail elsewhere [7]. Briefly, all patients with a potential CVD-related death who were identified by screening death certificates of all deceased within the study region were validated by sending standardized questionnaires two to four weeks after the date of death to the last attending physician and/or coroner (response rate >90%). From all those patients who died in the Klinikum Augsburg during the first 24 h from presumed beginning of symptoms (n = 2,076) we took a 19% random sample (n = 391) for an intensified validation process similar to that adopted in the prospective study. The study sample was divided into five 4-year periods (1985–1988, 1989–1992, 1993–1996, 1997–2000, 2001–2004). In the 204 patients with validated AMI according to the above-mentioned criteria, the same panel of three physicians also gave a judgment regarding the appropriateness of the therapeutic strategy by applying the same criteria and taking 'modern' infarction therapy as the basis.

Statistical Analysis

The associations between time periods and the judgment about the appropriateness of the therapeutic strategy were examined using logistic regression, while modeling time periods as an 11-level categorical variable simultaneously adjusting for age and sex and giving the p for trend. p values <0.05 were considered as statistically significant. Due to the low numbers, we decided not to present the data separately for men and women. All analyses were carried out with the SAS® system for Windows release 9.1.

Results

Classification and Timing of In-Hospital Deaths

During the observation period, 3,736 patients were identified who died in the Klinikum Augsburg. After exclusion of 2,384 patients who died >24 h after hospitalization – with the exception of patients originally hospitalized with a diagnosis other than CVD who died in hospital due to a presumable CVD death ≤24 h after symptom onset – 1,352 patients remained who died ≤24 h. Those were screened for a potential underlying cardiovascular cause of death. This is graphically illustrated in figure 1.

After first screening to exclude patients who clearly had died of causes other than CVD, 117 patients remained

Table 1. Characteristics of early deceased patients with a validated AMI (n = 79)

	n	%
Age, years (mean)	70.9 ± 9.6	–
Sex, male	50	63.3
Medical history		
History of hyperlipidemia	47	59.5
History of diabetes	43	54.4
History of hypertension	62	78.5
Active smoking	8	10.1
History of coronary artery disease	37	46.8
Previous myocardial infarction	26	33.8
History of cerebrovascular disease	17	21.5
History of peripheral artery disease	14	17.7
History of chronic pulmonary disease	9	11.4
History of malignant tumor	15	19.0
Known EF <40%	17	21.5

Table 2. Place of in-hospital death

All patients (n = 79)	n	%
Emergency room	23	29.1
Coronary care unit	38	48.1
General ward	16	20.3
During coronary intervention	1	1.3
During CABG surgery	1	1.3

Table 3. Reasons for withholding CPR

All patients without CPR (n = 29)	n	%
Multimorbidity	12	41.4
Hypoxic encephalopathy	3	10.3
Only catecholamines	12	41.4
Found dead with significant time elapsed after dying	2	6.9

Table 4. Judgment about appropriateness of therapeutic strategy

All patients (n = 79)		%
Other strategy might have been more successful[1]	1	1.3
No better strategy available because no stable circulation at any time (ongoing CPR)[2]	48	60.8
No better strategy, because best available strategy has been provided or was not indicated (e.g. multimorbidity)[3]	29	36.7
No judgment possible	1	1.3

[1] Patient was hospitalized with non-ST-elevation MI with, however, high-risk features (dynamic ECG-changes, diabetes and ongoing chest pain), but the performance of early coronary angiography was missed.

[2] Performance of CPR was considered optimal, further strategies like invasive coronary investigation and/or emergency application of extracorporeal circulatory support was deemed inappropriate/impossible.

[3] Patients who died despite optimal therapy or patients where notations in charts or interview of death-bystanders revealed severe multimorbidity or strong hints for the presence of hypoxic encephalopathy.

for intensified evaluation, resulting in 79 patients who were deemed to have AMI as the death-causing event (49 with definite, 17 with probable, and 13 with possible fatal AMI).

Characteristics of Early Deceased Patients with a Validated AMI

The age range was from 41 to 84 years (mean 70.9 ± 9.6), 50 were male (63.3%). Table 1 shows the characteristics of the patients. While 13 (16%) patients were already hospitalized, the majority (83%) came into hospital by the emergency system, with the exception of one patient who came to the emergency department by himself.

Patients Already Hospitalized (n = 13). The original reason for hospitalization was stable coronary artery disease in four patients, peripheral artery disease in four patients, diabetes mellitus in three patients, and abdominal surgery in two patients.

Patients Hospitalized by Emergency System (n = 65). From all patients who originally reached the hospital by the emergency system, the initial ECG derived by the emergency team showed ventricular fibrillation or flutter in 18 (28%) patients, and in 13 (20%) of patients asystolic or pulseless electrical activity. Forty-three (66%) patients had a prehospital cardiac arrest or cardiogenic shock, and in 37 (57%) prehospital CPR attempts have been made (CPR duration: mean 36 ± 12 min, median 40 min). In 32 cases with prehospital CPR, information about time from cardiac arrest until beginning of CPR attempts were available: in 24 (75%) of these patients the presumed time period from onset of cardiac arrest to arrival of professional medical help was less than 10 min.

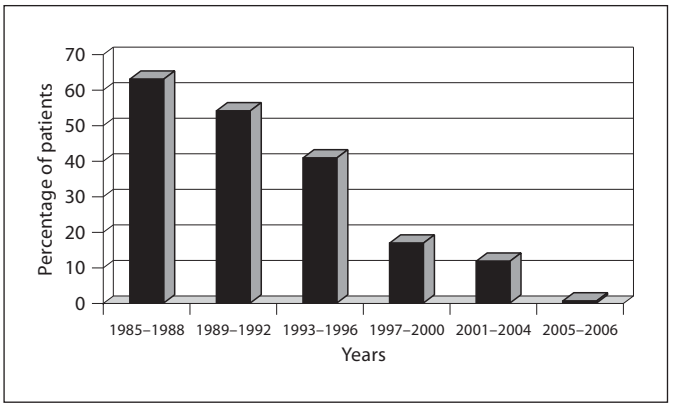

Fig. 2. Appropriateness of therapeutic strategy. Proportion of patients where an independent panel of clinicians judged that another therapy option would have been possible, based on modern AMI treatment strategies.

All Patients

In 60 patients (76%), a 12-lead ECG shortly before death was available (cases with no ECG were due to ongoing resuscitation attempts or in those found dead with significant time elapsed after dying). Most had ST elevation (46%) or bundle branch block (32%). Table 2 shows the place where death occurred.

In 50 patients (63%) CPR attempts were provided in-hospital. The reasons for withholding CPR for the other 29 patients are given in table 3. The most common reasons were multimorbidity or strong hints for hypoxic encephalopathy (51%). Treatment 'only with catecholamines' means that patients were treated in the CCU only with catecholamines without additional mechanical or electrical CPR activities because they were supposed to have no chance for myocardial recovery, including those patients who have been already revascularized or treated with an intra-aortic balloon pump.

In only 18 (23%) patients could a coronary angiography be performed, with primary PCI in 11/18 and emergency CABG in 3/18. In 6 patients (8%) thrombolyis (prehospital or early-inhospital) was provided; 9 (11%) patients were treated with intra-aortic balloon pump. In 24 patients an echocardiogram shortly before death was obtainable, where 15 patients showed a severely impaired global contractile function, 3 patients a hemodynamically significant pericardial effusion, and 1 patient a ventricular septal defect.

Evaluation of the patient history revealed that 34% had a previous MI and 21% had a previously documented EF <40% (with and without a history of previous MI). Of note, 26 patients (33%) had typical or atypical chest pain the days before the lethal event, four of those did refuse further diagnostic workup.

Table 4 gives the judgment about appropriateness of therapeutic strategy given by an independent panel of clinicians.

The same panel also retrospectively judged about the appropriateness of therapy from a sample of validated ≤24-hour in-hospital AMI deaths in 25- to 75-year-old patients in the years 1985–2004 (n = 203) using the same criteria while taking modern infarction management as the basis. Accordingly, an optional other therapy was judged to have been possible in 63, 54, 41,17 and 12% of patients for the years 1985–1988, 1989–1992, 1993–1996, 1997–2000, and 2001–2004, respectively (logistic regression analysis $p < 0.001$ for trend; fig. 2).

Discussion

While, over recent years, a decrease of in-hospital mortality could be shown in many clinical studies as well as registries, the magnitude was small due to a low baseline mortality of AMI patients who reached the hospital [3]. Numerous clinical trials, directed to improve in-hospital mortality, resulted in only small percentage mortality reductions, e.g. from 3.1 to 2.1% absolutely, due to the strict inclusion criteria [5].

By using another approach of prospective case finding and classification, we [9] as well as others [12] could show that the real in-hospital AMI case fatality is higher than supposed because – due to the fact of missing data classifying those deaths as AMI related – in most studies early occurring deaths are not counted. In an earlier retrospective analysis we were able to show that the decrease of early in-hospital deaths was particularly responsible for the tremendous fall in 28-day case fatality over the last 20 years which, however, still amounts to 11% [9]. The question remains whether under modern circumstances and therapy there are still options for improvement in early deceased patients not included in clinical trials or many registries. In the present study, we prospectively identified all early fatal possible AMI cases, analyzed the characteristics of these cases and potential other treatment options. Due to the prospective nature of the study and the application of very strict ascertainment criteria by timely investigation of all in-hospital cases of deaths, we could be certain not to miss any CHD-related deaths, and to optimally reveal the circumstances of death, allowing valid data for a clear classification of deaths as well

as identification of severity, therapy or potentially missed therapy. To our knowledge, we are the first to use such a comprehensive and timely investigation of presumed early in-hospital CHD-related deaths.

Although in the emergency setting it is often difficult to obtain valid clinical and electrocardiographic data, we could show that most of the patients with interpretable ECGs had ST elevation or bundle branch block AMI, underscoring the importance of these ECG manifestations as a high-risk feature, especially in the acute phase [14, 15].

In this prospective evaluation, we could confirm the trend seen in our earlier retrospective investigation that the proportion of very-high-risk patients – i.e. those with prehospital resuscitation or cardiogenic shock – was high and increased over time, suggesting that only those who died had no meaningful therapeutic option. This is underscored by the fact that, although most of the patients were under direct medical supervision (77% died either in the emergency room or on the coronary care unit), only 23% could be transferred to coronary angiography with consecutive revascularization attempts. The other patients either were under continuous resuscitation and could not be stabilized enough to get them into the cathlab or were patients in whom no CPR attempts have been provided (37% of all patients). In the latter the most common reasons why no CPR was attempted were multimorbidity or clinical judgment of no chance for recovery. We are not aware of similar investigations in the in-hospital setting. In a prospective study investigating all sudden cardiac deaths, the proportion of patients where no CPR attempts have been undertaken was 33%; however, most of the deaths occurred out of hospital, and only 53% were witnessed. Therefore, detailed information about circumstance of deaths and reasons for withholding CPR were not available [16]. Of note, although a significant number of early occurring in-hospital deaths were cases who were survivors of an out-of-hospital cardiac arrest, the present study was not a primary investigation about out-of-hospital-cardiac-arrest survivors, which would require another study design and is beyond the scope of the present article.

Of interest, taking all this information together, the judgment about appropriateness of therapeutic strategy given by an independent panel of clinicians revealed that only in one patient would another strategy have been promising, and the comparison with a retrospectively collected sample of early deaths revealed that this proportion dramatically decreased during the last 22 years. The most common reason for judging particular medical care cases during the previous 22 years to be inappropriate was missing early invasive therapy in patients presenting with cardiogenic shock or after prehospital resuscitation where it would have been reasonable [17] as well as possible (no ongoing CPR at presentation; data not shown). This also can be seen in our earlier analysis of the overall MI population where, for example, it could be shown that PCI procedures were performed in 30% in 1998 as compared to 66.0% in 2004 [18].

This observation allows two different interpretations: first, the dramatic fall in in-hospital mortality may largely be due to improvements in the acute care of critically ill patients in the early phase, and, in fact, earlier analysis from our studies showed that 28-day case fatality from in-hospital cases, when using validated clinical AMI criteria, decreased from 23% in 1985/1986 to 11% in 2005/2006 [7]. Secondly, nowadays – in the setting of a well-organized tertiary care centre – there seems to remain little space for further improvements beyond the established primary PCI strategy and optimal therapy for cardiogenic shock in CPR survivors [18]. On the other hand, it remains to be proven whether the more widespread application of more advanced mechanical circulatory support systems (including extracorporeal life support [19]), which were rarely applied in our institution and were not considered an appropriate treatment option in the investigated population, may add to further mortality reductions. We have no data about the appropriateness of CPR measures in the 57% of patients with prehospital CPR. However, the fact that the presumed time period from onset of cardiac arrest to arrival of professional medical help was less than 10 min in 75% of cases is in concordance with German law demanding arrival of emergency personal in less than 15 min in the majority of cardiac patients. This may indicate the effectiveness of the region's emergency system and also be due to the fact that the majority of prehospital cardiac arrests were witnessed.

On the other hand, the fact that 33% of the deceased patients have had typical or atypical angina pectoris complaints the days before the lethal event and four of those did refuse further diagnostic workup is alarming, and contradicts previous assumptions of sudden death patients who were assumed to mainly have been asymptomatic before the lethal event [20]. Accordingly, improvements in public and professional education about alarming symptoms indicating a need for immediate workup may be possible.

Limitations

It may be argued that the judgment about appropriateness of therapy is prone to be subjective. However, there

was an objective catalogue of criteria given to the panel, helping them to make their judgment as objective as possible. However, we cannot exclude the possibility that the judgment of the retrospective data may be more biased because timely information was less available and less complete than in the prospectively gained data. Despite a high percentage of available information about the circumstances of death, we cannot rule out that information regarding previous complaints about angina in the days before the lethal event is incomplete, and the number of 33% with typical or atypical angina pectoris complaints could be an underestimate. Finally, the upper limit of age was 85 years, and we have no data about numbers and potentially missed opportunities in this very old age group.

Conclusions

AMI patients with an early occurring in-hospital death have a pre-existing high-risk profile with pre-hospital cardiac arrest or cardiogenic shock in 66%. There are barely any options for improvement in acute care in these patients in the investigated setting (tertiary care centre). In 37% of the patients, there were no in-hospital CPR attempts undertaken for understandable reasons. In the view of primary prevention, however, in about one third of these patients earlier diagnostic and therapeutic measures might have been reasonable.

Funding Sources

This work was supported by a grant from the Deutsche Herzstiftung, Frankfurt a.M., Germany. The KORA research platform and the MONICA Augsburg studies were initiated and financed by the Helmholtz Zentrum München – German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research and by the State of Bavaria. Since 2000, the acquisition of data in acute myocardial infarction patients is co-financed by the German Federal Ministry of Health and Social Security to provide population-based myocardial infarction morbidity and mortality data for the official German Health Report (see www.gbe-bund.de). Steering partners of the MONICA/KORA Augsburg Infarction Registry are the KORA research platform, Helmholtz Zentrum München and the 1. Medizinische Klinik, Herzzentrum Augsburg-Schwaben, Klinikum Augsburg.

Acknowledgements

We would like to thank all members of the Helmholtz Zentrum München, Institute of Epidemiology, the field staff in Augsburg and the physicians who were involved in the planning and conduct of the study. We wish to thank the local health departments and the family physicians of the study area as well as the clinicians of the involved hospitals for their continuous support.

References

1 Furman MI, Dauerman HL, Goldberg RJ, Yarzebski J, Lessard D, Gore JM: Twenty-two year (1975 to 1997) trends in the incidence, in-hospital and long-term case fatality rates from initial Q-wave and non-Q-wave myocardial infarction: a multi-hospital, community-wide perspective. J Am Coll Cardiol 2001;37:1571–1580.

2 Masoudi FA, Foody JM, Havranek EP, Wang Y, Radford MJ, Allman RM, Gold J, Wiblin RT, Krumholz HM: Trends in acute myocardial infarction in 4 US states between 1992 and 2001: clinical characteristics, quality of care, and outcomes. Circulation 2006;114:2806–2814.

3 Rogers WJ, Frederick PD, Stoehr E, Canto JG, Ornato JP, Gibson CM, Pollack CV Jr, Gore JM, Chandra-Strobos N, Peterson ED, French WJ: Trends in presenting characteristics and hospital mortality among patients with ST elevation and non-ST elevation myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008;156:1026–1034.

4 Kuch B, Bolte HD, Hörmann A, Meisinger C, Löwel H: What is the real hospital mortality from Acute Myocardial Infarction? Epidemiological vs. clinical view. Eur Heart J 2002;23:714–720.

5 Stone GW, Brodie BR, Griffin JJ, Costantini C, Morice MC, St Goar FG, Overlie PA, Popma JJ, McDonell J, Jones D, O'Neill WW, Grines CL: Clinical and angiographic follow-up after primary stenting in acute myocardial infarction: the Primary Angioplasty in Myocardial Infarction (PAMI) stent pilot trial. Circulation 1999;99:1548–1554.

6 Fox KAA, Steg PG, Eagle KA, Goodman SG, Anderson FA, Granger CB, Flather MD, Budaj A, Quill A, Gore JM; GRACE Investigators: Decline in rates of death and heart failure in acute coronary syndromes, 1999–2006. JAMA 2007;297:1892–1900.

7 Kuch B, von Scheidt W, Ehmann A, Kling B, Greschik K, Hörmann A, Meisinger C: Extent of the decrease of 28-day case-fatality of hospitalized patients with acute myocardial infarction over 22-Years: epidemiological vs. clinical view. The MONICA/KORA Augsburg Infarction Registry. Circ Cardiovasc Qual Outcomes 2009;2:313–319.

8 Myerburg RJ: Scientific gaps in the prediction and prevention of sudden cardiac death. J Cardiovasc Electrophysiol 2002;13:709–723.

9 Löwel H, Lewis M, Hörmann A, Keil U: Case finding, data quality aspects and comparability of myocardial infarction registers: results of a South German register study. J Clin Epidemiol 1991;44:249–260.

10 The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. WHO MONICA Project Principal Investigators. J Clin Epidemiol 1988;41:105–114.

11 Luepker RV, Apple FS, Christenson RH, Crow RS, Fortmann SP, Goff D, Goldberg RJ, Hand MM, Jaffe AS, Julian DG, Levy D, Manolio T, Mendis S, Mensah G, Pajak A, Prineas RJ, Reddy KS, Roger VL, Rosamond WD, Shahar E, Sharrett AR, Sorlie P, Tunstall-Pedoe H: Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. Circulation 2003; 108:2543–2549.
12 Packham C, Gray D, Weston C, Large A, Silcocks P, Hampton J: Changing the diagnostic criteria for myocardial infarction in patients with a suspected heart attack affects the measurement of 30 day mortality but not long term survival. Heart 2002;88:337–342.
13 Stone GW, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Kornowski R, Hartmann F, Gersh BJ, Pocock SJ, Dangas G, Wong SC, Kirtane AJ, Parise H, Mehran R; HORIZONS-AMI Trial Investigators: Bivalirudin during primary PCI in acute myocardial infarction. N Engl J Med 2008;358: 2218–2230.
14 Kuch B, von Scheidt W, Kling B, Heier M, Hörmann A, Meisinger C: Characteristics and outcome of patients with acute myocardial infarction according to presenting electrocardiogram (from the MONICA/KORA Augsburg Myocardial Infarction Registry): Am J Cardiol 2007;100:1056–1060.
15 Sgarbossa EB, Pinski SL, Topol EJ, Califf RM, Barbagelata A, Goodman SG, Gates KB, Granger CB, Miller DP, Underwood DA, Wagner GS: Acute myocardial infarction and complete bundle branch block at hospital admission: clinical characteristics and outcome in the thrombolytic era. GUSTO-I Investigators. Global Utilization of Streptokinase and t-PA (tissue-type plasminogen activator) for Occluded Coronary Arteries. J Am Coll Cardiol 1998;31:105–110.
16 Chugh S, Jui J, Gunson K, Stecker E, John B, Thompson B, Ilias N, Vickers C, Dogra V, Daya M, Kron J, Zheng ZJ, Mensah G, McAnulty J: Current burden of sudden cardiac death: multiple source surveillance versus retrospective death certificate-based review in a large US community. J Am Coll Cardiol 2004;44:1268–1275.
17 Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, LeJemtel TH: Early revascularization in acute myocardial infarction complicated by cardiogenic shock. N Engl J Med 1999;341:1625–1634.
18 Kuch B, Heier M, von Scheidt W, Kling B, Hoermann A, Meisinger C: 20-year trends in clinical characteristics, therapy and short-term prognosis in acute myocardial infarction according to presenting electrocardiogram: the MONICA/KORA AMI Registry (1985–2004). J Intern Med 2008;264:254–264.
19 Samuels LE, Darzé ES: Management of acute cardiogenic shock. Cardiol Clin 2003;21:43–49.
20 Myerburg RJ, Interian A Jr, Mitrani RM, Kessler KM, Castellanos A: Frequency of sudden cardiac death and profiles of risk. Am J Cardiol 1997;80(5B):10F–19F.