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Original Article

Comorbidities in relation to fatality of first myocardial infarction

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ABSTRACT

Introduction: Present knowledge concerning potential associations between comorbidities and the fatality of a first myocardial infarction (MI) is limited.
Aim: To identify comorbidities in 45–70-year-old individuals who suffered a first MI and died within 7 days in Stockholm County from 1992–1994. In addition, to assess how each of the comorbidities identified, as well as the number of hospitalizations during the 10-year period prior to the MI, was associated with MI fatality.
Methods: The data collected on our inception cohort of 1984 first MI, of which 524 were fatal within 7 days, were primarily self-reported, proxy-reported by questionnaire and/or extracted from comprehensive national registers. Comorbidities among fatal cases with a prevalence >2% were identified. Risk ratios (with 95% confidence intervals) for the association of MI fatality with number of prior hospitalizations and specific comorbidities were calculated using binomial regression with log link. A structured review of autopsy reports on fatal cases was performed in order to identify additional indicators of comorbidities.
Results: After adjusting for sex, age and disposable income, the number of previous hospitalizations was associated with 7-day MI fatality. Of the comorbidities identified as prevalent in fatal cases, the following were associated with 7-day fatality in crude analysis: epilepsy, heart failure, stroke, alcoholism, cancer, renal diseases, asthma, psychiatric diseases, diabetes, and rheumatoid arthritis. Indicators of comorbidities identified from autopsy data included a silent MI, severe atherosclerosis of the abdominal aorta, and hepatic steatosis. Adjustments for sex and age (although not possible for epilepsy and alcoholism), did not substantially alter results.
Conclusions: Our current findings indicate that in connection with a first MI, particular attention should be paid to those with repeated prior hospitalizations and/or epilepsy, heart failure, stroke, alcoholism, cancer, renal diseases, asthma, psychiatric diseases, diabetes and rheumatoid arthritis.

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1. Introduction

Although fatality from coronary heart disease (CHD) is declining in various populations [1–4], 25%–35% of those who suffer a coronary event still die within 28 days [1–3], with the vast majority of cases occurring outside of the hospital [1,3–5]. Our knowledge concerning determinants of death from myocardial infarction (MI) is presently limited, although the presence of comorbidity (usually defined as a medical condition existing simultaneously with, and independent of, another medical conditions), is likely to be a risk factor for dying during the acute phase following an MI [6]. Previous studies that took both in- and out-of-hospital deaths into consideration, which may be referred to as population-based studies, focused on selected comorbidities, such as diabetes [4,7–10], hypertension [7,9–12], hyperlipidemia [7,12], arrhythmias [4,13] and angina [4,13] and arrived at different conclusions regarding the associations of such conditions with MI fatality. Previous hospitalizations due to severe and/or multiple comorbidities may be especially associated with MI fatality. However, no population-based study has yet assessed how the number of previous hospitalizations is related to MI fatality, nor presented a comprehensive overview of earlier diagnoses in individuals who have suffered a fatal coronary event. In addition, only a few earlier investigations in this area have had access to registers documenting diagnoses in connection with previous hospitalizations in combination with questionnaires covering diseases that usually do not require admission to hospital [7,9,11,13].

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The overriding aim here was to improve our understanding of how presence of comorbidities may influence fatality from a first MI in the general adult population. Specifically, we explored (1) the association between the number of hospitalizations during a 10-year period prior to the MI and death within 7 days afterwards, (2) which comorbidities are most prevalent among cases of fatal MI, and how these are associated with such fatality, and (3) whether autopsy findings on individuals whose first MI was fatal indicate the presence of co-morbidities other than those identified from other data. This investigation was based on cases of MI identified in connection with the Stockholm Heart Epidemiology Program (SHEEP) performed between 1992 and 1994 – a period during which approximately 70% of all deaths from MI among 45–70-year-old residents in Stockholm were confirmed by autopsy [7]. Information on comorbidities was available from questionnaires, as well as national registers. In addition, autopsy reports provided a unique source of data concerning pathological findings associated with fatal first MI.

2. Material and methods

2.1. Study population

This study is based on material from the Stockholm Heart Epidemiology Program (SHEEP) which was designed to increase our knowledge concerning the influence of various risk factors on the occurrence of and prognosis for MI among male and female Swedish citizens 45–70 years old and residing in Stockholm County. MI was defined with the following criteria: (i) certain symptoms according to anamnesis, (ii) specified changes in serum activity of the creatinine kinase and lactose dehydrogenase, (iii) specified ECG-changes and (iv) autopsy findings. The MI diagnosis required two of the criteria (i–iii) to be met, or that autopsy findings showed myocardial necrosis of an age compatible with the time of disease onset. Eligible for inclusion in our inception cohort were all members of this population who suffered their first MI between 1992 and 1994.

Details concerning the identification of cases of MI in connection with SHEEP have been reported previously [14]. In brief, 2246 cases of first-time, documented MI were identified from three sources: (1) coronary units and internal medicine wards for acute care in all Stockholm hospitals; (2) the Swedish National Patient Register; and (3) death certificates. In the original SHEEP study, fatal MI was defined as death within 28 days following initial symptoms.

Our primary analyses considered fatal cases as those who died out-of-hospital (n=203), in the emergency ward (n=170), or in-hospital within 7 days after the onset of MI (n=151), for a total n=524, referred to hereafter as 7-day fatal cases. In-hospital deaths occurred either in intensive care units (n=59), internal medicine wards (n=35) or other wards (n=57). Thus, MI fatality was defined primarily as the proportion of all those who suffered their first MI and died within 7 days after diagnosis, as well as, secondarily, the proportion that died within 28 days. Among the 7-day fatal cases who were hospitalized and for whom clinical log data were available (n=42), the median hospitalization time was 3 days (interquartile range 2–5 days). For non-fatal cases (n=1460) for whom clinical log data were available (n=1272), the corresponding figure was 6 days (interquartile range 5–8 days).

3. Sources of data

3.1. Questionnaire data

Non-fatal cases filled in a questionnaire containing a general question concerning any pharmacological treatment during the week preceding the MI and, if so, the purpose for. In addition, these individuals were asked about the occurrence of angina, heart failure, stroke, intermittent claudication, diabetes, hypertension and/or hyperlipidemia at any time before the index event. This questionnaire also encompassed lifestyle, height, weight, psychosocial environment, occupational-related exposures and family history of disease. An analogous questionnaire concerning the fatal cases was administered to their close relatives (proxies). The participation rate among non-fatal cases and proxy respondents was 86% and 63%, respectively.

3.2. Information from the National Patient Register

The National Patient Register [15], with complete coverage in Stockholm County since 1975 and nationwide since 1987, provided both the primary and secondary diagnoses (of which as many as seven were taken into consideration) for all cases of MI included in the SHEEP [15]. The 10-year period preceding the MI event was examined here. On the basis of the National Patient Register, the number of hospitalizations during these 10 years (0 = the reference category, one, two or three or more), excluding routine child delivery, was determined.

3.3. Autopsy reports

The proportion of 7-day fatal cases that underwent autopsy, as documented in death certificates, was 72%. From county council archives (mainly for Stockholm County) and from departments of forensic medicine (all in Stockholm, except from one autopsy that took place in Uppsala), we retrieved 49% (n=186) of the reports on these autopsies, of which 37% were performed at a department of forensic pathology.

The historical summaries available in 95% of these autopsy reports were used to identify comorbidities in fatal cases for which questionnaire data were not available. In the case of clinical pathology autopsies, these summaries were based on short medical reports written by the doctor who requested the autopsy and were compiled before the external and internal examinations took place. With forensic autopsies, these are based primarily on police interviews of close relatives or acquaintances of the deceased, as well as to some extent on medical reports, whenever available. In addition, the findings from the external and internal autopsy examinations were reviewed for indicators of additional comorbidities in a structured manner, as shown in the S1 Text.

3.4. Additional variables

Low disposable income, defined previously [7], was considered a potential confounder.

3.5. Statistical analysis

On the basis of the National Patient Register and SHEEP questionnaire, we assessed the prevalence of all comorbidities in the group who suffered a fatal MI. Whenever the SHEEP questionnaire was not available, the historical summaries in the autopsy reports, if available, were used instead. Certain of the comorbidities considered, such as asthma, were defined narrowly and identified with a single ICD-8/ICD-9 code whereas the majority, including psychiatric diseases, were broadly defined as described in S2 Table. All comorbidities thus identified were considered, but for statistical reasons, only those with a prevalence of at least 2% were evaluated further. We assessed the prevalence of the corresponding comorbidities in the non-fatal cases in the same manner. For descriptive purposes, we calculated the age- and sex-standardized prevalence of the comorbidities in fatal cases, using non-fatal cases as reference.

Obesity, defined as a BMI (calculated as previously described [16]) of 30 kg/m^2 or higher, was identified as previously reported [7].

To assess the association between each of the individual and groups of comorbidities identified and MI fatality, we calculated risk ratio (RR) point estimates with 95% confidence intervals (CI) for MI fatality using binomial regression with a log link. The RR is a ratio between the fatality of those with and without a specific comorbidity. We evaluated the

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