

Pre-Hospital Decision Process and Prognosis in Men and Women with Coronary Heart Disease

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"Utän tvivel är man inte klok"
- Tage Danielsson

To my family

ABSTRACT

The overall aim of this thesis was to describe experiences, strategies and actions in the prehospital phase among patients with a first acute myocardial infarction and to examine long-term trends in survival among patients with coronary heart disease.

The thesis consists of two qualitative and two quantitative studies. Interviews were conducted with 21 men and 17 women, experiencing symptoms from a first acute myocardial infarction (AMI) and analyzed with Grounded Theory. Two national prospective cohort studies were performed by using the Swedish Inpatient register (IPR). From this, prognosis for 37,276 adult patients <55 years old with a first AMI and 94,328 patients aged >18 years who underwent a first coronary artery bypass (CABG) 1987-2006 could be estimated.

During the decision process, various spectra of bodily changes were described in both men and women, sometimes over an extended period before submission to hospital. Intermittent, vague and insidious symptoms caused confusion about how to act. Vague symptoms sometimes experienced by the men did not match their preconception of typical symptoms in a myocardial infarction. To come to an understanding they compared with their past experiences which led to an awareness of the abnormality, the severity and the need for contact medical attention. The women usually attributed their symptoms to harmless conditions and struggled to continue with their responsibilities in their daily lives. Intensified symptoms made the women unable to perform their daily task and they could no longer maintain earlier explanations for their discomfort which contributed to an understanding for the need of professional help. Sometimes, when men and women sought medical attention for their discomfort, and had no objective signs of an AMI they were dismissed, with no diagnosis, which caused a hesitation to contact medical care once again. This emphasizes that health care professionals have to pay more attention to the patient's narrative.

In the quantitative part of the thesis younger men with a first AMI had a 2 to 4-fold risk for mortality compared to men in the same age in the general population while women had a 6 to 14-fold risk during the last study period (2002-2006). Survival increased during the study period in men. In women there was a favorable trend in survival until the last period 2002-2006 but survival then reverted to that in the second period (1992-1996) in the last period. Men and women ≥ 55 years surviving the first 30 days after CABG (coronary artery bypass grafting) showed a lower mortality risk than those in the general population and showed a decreasing trend in mortality during the study period. Women below the age of 55 showed no significant improvement in survival and had a 4-fold risk for mortality compared to women in the same age in the general population. Men <55 displayed improved survival, which was higher than that for men in the general population.

Keywords: acute myocardial infarction, decision-making process, experiences, grounded theory, epidemiology, mortality, survival, coronary artery bypass grafting, temporal trends.

LIST OF PAPERS

This thesis is based on the following papers, referred to the text by their Roman numerals I-V:

- I Nielsen, S., Falk, K., Gyberg, A., Määttä, S., Björck, L. Experiences and Actions During the Decision Making Process Among Men With a First Acute Myocardial Infarction.
Journal of Cardiovascular Nursing 2014. [Epub ahead of print]
- II Gyberg, A., Björck, L., Nielsen, S., Määttä, S., Falk, K. Women's help-seeking behavior during a first acute myocardial infarction.
Submitted
- III Nielsen, S., Björck, L., Berg, J., Giang, KW., Zverkova Sandström, T., Falk, K., Määttä, S., Rosengren, A. Sex-specific trends in 4-year survival in 37 276 men and women with acute myocardial infarction before the age of 55 years in Sweden, 1987–2006: a register-based cohort study.
BMJ Open 2014;4(5)
- IV Nielsen, S., Björck, L., Jeppsson, A., Giang KW., Falk, K., Määttä, S., Zverkova Sandström, T., Rosengren, A. Trends in absolute and relative mortality risk in 94 328 patients surviving 30 days after a first isolated coronary artery bypass graft procedure 1987-2006. A population based study.
In manuscript

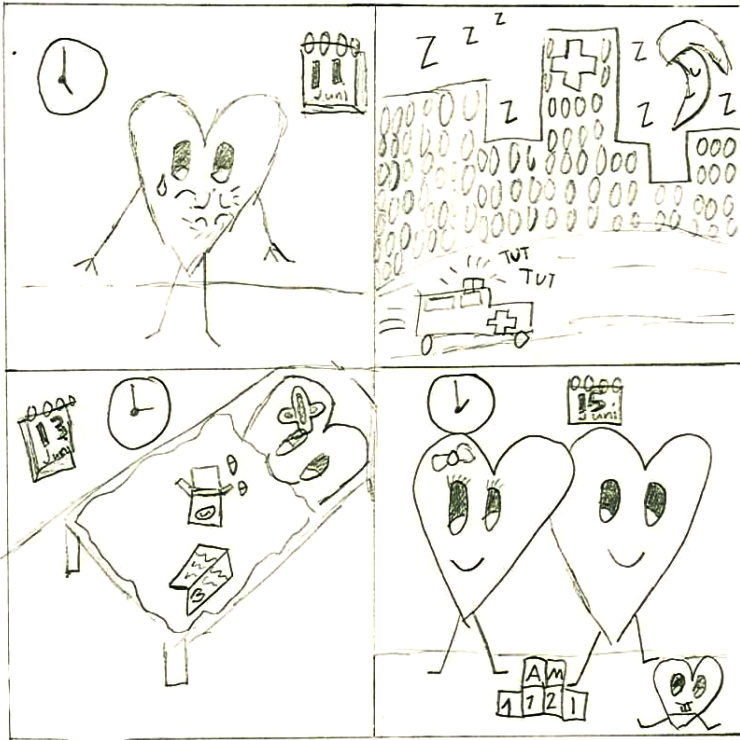
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ABBREVIATIONS

| | |
|--------|--|
| ACE | Angiotensin Converting Enzyme |
| ACS | Acute Coronary Syndrom |
| AER | Absolute Excess Risk |
| AMI | Acute Myocardial Infarction |
| AR | Absolute Risk |
| CABG | Coronary Artery Bypass Grafting |
| CCU | Coronary Care Unit |
| CHD | Coronary Heart Disease |
| CI | Confidence Intervals |
| CK-MB | Creatine Kinase Myocardial Band |
| CVD | Cardiovascular Disease |
| ECC | Extra Corporeal Circulation |
| ECG | Electrocardiogram |
| HR | Hazard Ratio |
| ICD | International Classification of Diseases |
| IHD | Ischemic Heart Disease |
| IPR | Inpatient Register |
| NSTEMI | Non ST-elevation Myocardial Infarction |
| PCI | Percutaneous Coronary Intervention |
| PPV | Positive Predictive Value |
| SCB | Statistiska Central Byrån |
| SMR | Standardadised Mortality Ratio |
| STEMI | ST-elevation Myocardial Infarction |



ELLA NIELSEN

INTRODUCTION

Coronary artery disease

The mortality from coronary heart disease (CHD) has decreased sharply during the last two decades. However, CHD is still the most common cause of death in Sweden and in the Western world.⁽¹⁾ The incidence of AMI in Sweden has also displayed a decreasing trend since the 1980s. In 2013 the number of AMI cases in Sweden was about 30,000.⁽²⁾

Pathophysiology of atherosclerosis

Atherosclerosis is a condition in which plaque builds up inside the arteries. Plaque is made of cholesterol, fatty substances, cellular waste products, calcium and fibrin.⁽³⁾ Atherosclerosis is the most common cause of myocardial infarction⁽⁴⁾. The process of atherosclerosis begins at an early age.^(5, 6) The process is not yet entirely understood but the current understanding is that fat infiltration starts an inflammatory process in the endothelium cells. Over time a lesion occurs composed of muscle cells and lipids covered by a fibrous cap (plaque). This plaque may gradually result in a narrowing of the coronary artery lumen.^(7, 8) The plaque can also be confined to the artery wall, with no effect on the lumen, and hence normal angiographic findings,⁽³⁾ sometimes reported to be more common in women.⁽⁹⁾

Angina pectoris

Symptoms of atherosclerosis in angina pectoris may occur in connection with physical activity or psychological stress. The increased oxygen demand when cardiac output increases cannot be satisfied through the affected coronary vessels which causes myocardial ischemia. However, this myocardial ischemia is temporary, typically improving when the demand of oxygen in the myocardium decreases, as in stable effort angina.^(10, 11)

Acute Coronary Syndrome

The concept of acute coronary syndrome (ACS) generally denotes a condition where thrombus forms over a disrupted a plaque caused by either an erosion or rupture.⁽¹²⁾ with a narrowing or occlusion of the vessel and myocardial ischemia as a result.⁽³⁾ The occlusion of the vessel lumen can be intermittent or permanent.⁽⁷⁾ The magnitude of the reduction of the blood flow and the presence of collateral vessels are two central factors which have an impact on the time to myocardial cell death.^(3, 13) Clinical diagnoses included in ACS are unstable angina, non-ST elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI).⁽¹²⁾ In 2012 Thygesen et al defined myocardial infarction as myocardial cell death due to prolonged ischemia.⁽⁴⁾ Further, myocardial infarction is categorized into five different types of classification with subgroups due to both pathological, clinical and prognostic factors: type 1) spontaneous myocardial infarction, type 2) myocardial infarction secondary to an

ischemic imbalance, type 3) myocardial infarction resulting in death when biomarker values are unavailable, type 4a) myocardial infarction related to percutaneous coronary intervention (PCI), type 4b) myocardial infarction related to stent thrombosis, type 5) myocardial infarction related to coronary artery bypass grafting (CABG).⁽⁴⁾

Diagnostic process

The diagnostic process for ACS (Figure 1) depends on three clinical key criteria: symptoms, electrocardiogram (ECG) indicating ischemia and biochemical markers.^(4, 12)

| Acute Coronary Syndrome | | |
|-------------------------|----------------------------------|------------------------|
| Symptoms | Symptoms | Symptoms |
| ST-elevation | ST/T abnormalities or normal ECG | Normal ECG |
| Positive biomarkers | Positive biomarkers | Normal biomarkers |
| ↓ | ↓ | ↓ |
| STEMI | N-STEMI | Unstable angina |

Figure 1. The diagnostic process of ACS.

Symptoms

There is a varied spectrum of reported symptoms in connection with ACS.⁽¹⁴⁾ Described symptoms are discomfort or pain in the chest, neck, jaw, arms or in the back. Other symptoms may be dyspnea, dizziness, syncope, fatigue, palpitations, dyspnea, vomiting and sweating.^(12, 15, 16) However, the predominant symptom in ACS is chest pain in both men and women.⁽¹⁷⁻¹⁹⁾ Studies which have examined gender differences in symptoms have reported that men present more often with chest pain than women.^(14, 20) However, Berg et al (2009) did not find any gender differences regarding chest pain.⁽¹⁸⁾ In addition, patients with STEMI are more likely to present with chest pain (43.6%) than patients with NSTEMI (27.1%).⁽²¹⁾ However, both women and men often have other symptoms such as pain from the upper abdomen, neck, jaw, dizziness and nausea, but previous research indicates that women report these symptoms to a greater extent than men.^(14, 18, 22, 23) Furthermore, prodromal symptoms are described by the literature as vague and intermittent symptoms during the time before admission to hospital with a diagnosis of AMI.^(24, 25)

Electrocardiogram

Criteria for ACS derive from which patterns are shown in the ECG. Signs of ischemia can be either significant changes in the ST segment-T wave, or new left bundle branch block or pathological Q-waves. In this respect, myocardial infarctions are classified into two main categories; ST elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI).⁽⁴⁾

Biochemical markers

Biochemical markers are used to detect a myocardial injury. In year 2001, new guidelines for a diagnosis of AMI were introduced⁽²⁶⁾ with a lower limit for CK-MB. In addition, more sensitive markers were introduced (troponin).^(27, 28)

Biochemical markers reflect a necrosis of the myocardial cells but do not give information of different clinical presentation of ACS or to other underlying causes. Increased troponin levels can also be due to other cardiac diseases than AMI such as heart failure and myocarditis but also to non-cardiac conditions such as renal failure, severe anemia and sepsis.^(4, 29)

Trends in incidence and mortality

The incidence of AMI in Sweden during 2013 among men and women aged >20 years was 482/100 000 in men and 313/100 000 in women, after an age-adjusted reduction in incidence of 36% since 2001.⁽³⁰⁾ Similarly favorable findings with declining trends in incidence in myocardial infarction was found in a large study from United States, with a decline of 20% from 2000 to 2008.⁽³¹⁾ Women experience their first AMI about 5-10 years later than men.^(32, 33) Data from a Swedish study showed a decreasing trend in the proportion of STEMI in favor of an increasing trend in NSTEMI. Further, the proportion of patients with STEMI was higher in men compared to women. In addition, it was also found that patients with STEMI had an increased risk for mortality compared to patients with NSTEMI.⁽³⁴⁾

Despite decreasing trends during the last thirty years CHD is still the leading cause of death.^(1, 35) In Sweden, the overall mortality with AMI as an underlying cause has decreased from 15,900 to 6,200 persons during the years 1990-2013.⁽³⁰⁾ A recently published Swedish study observed similar findings with declining trends in CHD mortality of 67.4% in men and 65.1% in women between 1987-2009.⁽³⁶⁾ Previous studies have also shown that the majority of all deaths related to CHD occur out of hospital.⁽³⁷⁾ Although studies have shown decreasing trends in CHD mortality,^(36, 38) other studies in men and women <55 years old showed a flattening trend in mortality due to CHD.^(39, 40) However, a recent published Swedish study could not confirm these trends among younger women and men in Sweden.⁽³⁶⁾

Risk factors for Coronary Heart Disease

The INTERHEART study showed that 90% of all myocardial infarction in both men and women could be explained by nine factors: smoking, lipids, hypertension, diabetes, abdominal obesity, psychosocial factors were associated with increased the risk of AMI while regular intake of fruits and vegetables, regular alcohol consumption and regular physical activity had a protective impact.⁽⁴¹⁾

Delay in seeking medical care

It is known that people hesitate to seek medical care when experiencing symptoms of

AMI despite the importance of rapid treatment of coronary artery occlusion to prevent morbidity and mortality.^(42, 43) In this context “patient delay” is essential. During the past decades, studies have showed that delay in time has been reduced^(44, 45) or remained unchanged.^(46, 47) However, one Swedish study showed an increasing trend in delay during the first 24 hours for both men and women during the period 1989 to 2003.⁽²⁰⁾

Patients’ delay in AMI is reported to be affected by clinical presentation. Patients with STEMI have shorter delay than patients with NSTEMI.⁽⁴⁸⁾ A Danish study investigated the associations between delay and mortality in patients with STEMI, demonstrating that the time from when patients contact emergency medical service (EMS) to PCI was associated with higher mortality (system delay). However, the time from onset of symptoms to contact with EMS (patient delay) was not associated with increased mortality.⁽⁴⁹⁾ Since a majority of all deaths related to CHD occurs out of hospital,⁽³⁷⁾ the impact that patient delay has on mortality may be underestimated. In addition, studies show that patients who report prodromal symptoms the days before the myocardial infarction have longer delay.^(24, 25)

Previous research shows conflicting results regarding which impact gender differences have on delay. Some studies has found that women have a longer delay than men^(44, 46, 47, 50, 51) while other studies found no gender differences.^(52, 53)

Several studies have examined the role of socio-demographic and clinical factors on the time from symptoms onset to hospital admission or treatment. Factors which prolong the delay are advanced age, lower income, previous AMI, history of diabetes, angina pectoris, heart failure and intermittent symptoms or absence of chest pain.^(21, 48, 50, 54, 55) However, one study did not found any significant differences regarding previous AMI and delay.⁽⁵⁶⁾

Further, reasons for delay can be explained by how people interpret their symptoms. Insidious symptoms or vague feelings of illness are quite common in both men and women but are not interpreted to be related to severe disease such as AMI.^(15, 57, 58) Additional reported reasons for hesitation in seeking medical care is worries to be a burden to relatives, colleagues or friends but also to the health care professionals.^(59, 60)

Treatment procedures

There are several medication therapies which have impact on the prognosis for patients with CHD,⁽⁶¹⁾ such as antiplatelet,⁽⁶²⁾ angiotensin converting enzyme inhibitors (ACE),⁽⁶³⁾ beta blockers,⁽⁶⁴⁾ statin therapy.⁽⁶⁵⁾

Two methods for revascularization in patients with CHD or acute ACS are CABG and PCI. These procedures restore the blood flow to the myocardium and aim to increase survival and relieve symptoms.⁽⁶⁶⁾ The technique in CABG aims to regain the blood flow to the myocardium by anastomoses beyond the lesion(s) while PCI techniques usually restore the native vessels.⁽⁶⁷⁾

Surgery interventions to relieve coronary stenosis started already in the beginning of the 19th century but it was not until 1960s that the methods in CABG became successful.^(66, 68, 69) The development of coronary angiography techniques had a great influence in refining methods in revascularization.⁽⁷⁾ At the end of the 1970s Andreas Gruentzig started a new invasive technique with a balloon catheter in order to expand a coronary stenosis.^(66, 69) Since then, PCI as a revascularization method has advanced rapidly.

Increased knowledge about revascularization methods has resulted into detailed guidelines aimed to guide clinicians and patients to select appropriate revascularization methods. This together with technological development of PCI and changes in criteria for revascularization methods has led to a shift with an increased proportion in PCI procedures and a decrease in CABG procedures.^(66, 70-72)

CABG is now the recommended method in patients with left main artery disease and/or three vessel coronary artery disease and diabetes while PCI is mainly used in patients with AMI presenting with ST-elevation⁽⁶⁷⁾ and in patients with non-STEMI, unstable angina and less extensive disease.

Few studies have investigated long-term mortality in patients with a first isolated CABG, but mortality within 30 days after CABG surgery has decreased during the last two decades.^(73, 74) The observed mortality rate decreased from 2.4% in 2000 to 1.9% in 2009.⁽⁷³⁾ Similar favorable trends in 30-day mortality are also shown in a Swedish report.⁽⁷²⁾ Some studies have shown higher mortality during the first 30 days after surgery in women compared to men,⁽⁷⁵⁻⁷⁷⁾ but there are also gender differences in patient characteristics among those who undergo CABG. Women are older and have more comorbidities such as diabetes, hypertension and hypercholesterolemia than men while smoking and previous myocardial infarction are more common in men.^(75, 77)

RATIONALE FOR THIS THESIS

Despite positive trends in incidence and mortality, there is still a large group of men and women who are affected by CHD in Sweden and globally. Continuous work is therefore warranted to identify experiences in men and women of the disease and trends in prognosis. Focus in this thesis is on how CHD affects the individual's life and changes in health regardless of clinical presentation.

Although there is an improved survival after an AMI during the past decades, a key factor for the prognosis is early treatment. Rapid treatment reduces the damage of the heart muscle and prevents morbidity and mortality. Previous research shows that people sometimes hesitate to seek care for symptoms of AMI, however, the reasons for this hesitation are not fully understood. Each individual lives in a social context, interacting and affected by the surrounding world through its history, culture, language⁽⁷⁸⁾ which can have an impact on experiences and acting in the decision to seek care. There is a need for increased knowledge and awareness of the decision process in the efforts to reduce the delay in time. By examine pre-hospital experiences, a deeper understanding of the hesitation to seek medical care can be identified.

During the last twenty years there have been changes in treatment, diagnostic criteria and clinical presentation in patients with AMI. Most studies have focused on prognosis in elderly patients with AMI. However, men and women below 55 years stand to lose more of their remaining life compared to older patients and there is a need for increased knowledge in prognosis among younger AMI survivors. Development of surgical technological advances during the last decades have contributed to changed criteria for revascularization methods for patients with CHD, which have resulted to a decline in the proportion of patients who undergo CABG surgery. In addition, few populationbased studies have been conducted regarding prognosis in younger individuals suffering from a first AMI or prognosis in survival after CABG surgery. It is accordingly, important to identify patterns and trends which may reflect effects of care and treatments over time with a potential impact in prognosis for patients with CHD. Increased knowledge about prognosis in survival for patients with CHD is important for the affected individuals and has an important clinical significance for health care professionals involved in the treatment of CHD.

AIMS OF THIS THESIS

The overall aim of this thesis was to explore the experiences, strategies and actions in the pre-hospital phase among patients with a first AMI and to examine long-term trends in survival among patients with CHD.

Specific aims

- I To describe the actions and experiences involved in the process of seeking medical attention in men with a first AMI.
- II To identify how women's experiences interacted and influenced the decision to seek medical care at their first acute myocardial infarction.
- III To examine sex-specific trends in long-term survival in a register-based cohort of patients aged 24–54 years hospitalized with a first AMI during 1987–2006, and to compare death rates for men and women separately with those of the general population.
- IV To examine trends in 4-year survival among men and women after a first isolated CABG during 1987 to 2006 and compare mortality rates in men and women in this study population to those of the general population.

ETHICAL CONSIDERATIONS

All studies were approved by the regional Ethics Committee in Gothenburg.

Paper I and II

All the participants were informed that their participation was voluntary and about the possibility to withdraw at any time without providing any reason. The protocol for Paper I and II was approved by the regional Ethics Board of Gothenburg. (Dnr: 352-11)

Paper III and IV

To avoid identification of participants and to ensure anonymity, all personal identifiers were removed and replaced with a sequential number in the dataset. The protocol for Paper III and IV was approved by the regional Ethics Board of Gothenburg. (Dnr: 540-11)

METHODS

Methodological approaches

This thesis involves analyses of both qualitative and quantitative data (Table 1). The different methodological approaches were used to broaden the knowledge and to identify different aspects of how changes in health affect men and women before and after hospitalization with CHD. Paper I and II aimed to increase the knowledge about the decision process to seek medical care among men and women experiencing their first AMI. Paper III and IV aimed to identify patterns in prognosis and changes over time in individuals living with CHD.

Table 1. Overview of the study designs and samples in each paper

| Study | Design | Data collection | Study population | Data analysis |
|-------|---|--|--|---|
| I | Explorative Descriptive | Interviews | 21 men diagnosed with a first AMI | Grounded Theory |
| II | Explorative Descriptive | Interviews | 17 women diagnosed with a first AMI | Grounded Theory |
| III | Descriptive population based register study | The Swedish Inpatient Register, Cause of Death Register | 37,276 women and men (<55 years) with a first AMI | Statistical analysis AR, AER, SMR, HR, KM |
| IV | Descriptive population based register study | The Swedish Inpatient Register, Cause of Death Register | 94,328 women and men who underwent first isolated CABG | Statistical analysis AR, AER, SMR, HR |

AR, Absolute Risk, AER, Absolut Excess Risk, SMR, Standardadised Mortality Ratio, HR, Hazard Regression, KM, Kaplan Meier.

Study population

International Classification of Diseases

The identification of all four study cohorts (Paper I-IV) was based according to diagnostic and procedural codes in the International Classification Diseases system (ICD) in all of the papers. The World Health Organization (WHO) became responsible for the ICD revisions in 1948. Since the start, this ICD system has been revised 10 times where the current version is the 10th revision.⁽⁷⁹⁾ In Sweden, ICD 8th codes were used until 1986, ICD 9th codes until 1996 with ICD 10th revision used from 1996 and onwards.

Paper I and II

The studies included 21 men and 17 women with a first AMI, (ICD-10; I21), hospitalized at any of the the coronary care units (CCU) at Sahlgrenska University Hospital,

Gothenburg, Sweden. The men were included between May 2011 and March 2013 and the women between June 2011 and May 2012. The patient records were used to identify participants with symptoms and clinical signs and a preliminary diagnosis code of AMI. The diagnosis code was verified in the discharge note and none of the participants were excluded on the basis of inaccurate diagnosis at discharge. Nurses at the CCU or research nurses gave oral and written information about the study and asked the patient whether they would like to participate. One man and one woman chose to not take part due to stressful life situations. An exclusion criterion for participation was inability to speak Swedish. A wide range in age criteria (25 to 75 years) was selected in order to grasp an open spectrum of varied experiences during the decision process regardless of age. The lower age limit were chosen in order to capture young participants. We set an upper limit of 75 because we wanted to avoid cognitive dysfunction. There was no selection criteria aimed at any specific patient delay. Instead the selection process was about the men and women's ability and interest to share their experiences, thoughts, actions and social processes irrespective of time from symptoms onset until the decision to seek medical care.

Paper III

In this population based prospective cohort study, 38,836 cases in Sweden aged 25-54 years, hospitalized with a first AMI in 1987-2006 were included. After excluding cases (1,560) who died during the first 28 days, 37,276 cases (7,229 women and 30,047 men) with a first AMI remained for analysis. AMI was defined as a principal discharge code according to the ICD-8 410 (until 1986); ICD-9 410 (until 1996) and ICD-10 I21 (from 1997 onward). In order to identify an event as a first AMI, data from 1980 and onwards were used. To ensure that all registered AMIs each year had the same chance of being identified as a first event, a time frame of 7 years throughout was used. Criteria for a diagnosis of AMI in Sweden have followed established guidelines, changing after the adoption of new AMI criteria in the year 2000. Thus, the characteristics of the AMIs in our analysis changed during the study period. Use of troponins became standard after the year 2000.

Paper IV

The inclusion procedure to find eligible patients was performed in two steps. First; International Classification of Diseases (ICD 9 and ICD 10) was used to find patients who received the principal codes ICD-9 410-414 and ICD-10 I20-I25. Second; surgical procedure codes for CABG ICD-9 3066, 3105, 3127, 3158, 3092, and ICD-10 FNA, FNB, FNC, FNE, FNF were used to identify patients who underwent a first isolated CABG. All procedures were included irrespective of the use of extra corporeal circulation (ECC) or off-pump techniques.

Between 1987 and 2010, a total of 96,488 patients who had undergone a first isolated CABG were identified. Of these 234 patients were excluded because there was no CHD diagnosis at hospital discharge (ICD-9 410-114 and ICD-10 I20-I25). After this exclusion the study cohort comprised 96,254 patients, of these, 1,926 patients (1,310 men and 616 women) died during the first 30 days. The remaining cohort consisted of

94,328 patients who had survived the first 30 days (74,113 men and 20,215 women). Out of this cohort 30,129 (31.9%) had undergone emergency CABG surgery, while 64,199 (68.0%) underwent elective procedures.

The study cohort was stratified into two age groups (18-54 years, ≥ 55 years). Further, the study cohort was stratified into four study periods (1987-1991, 1992-1996, 1997-2001 and 2002-2006) which allowed for an equal 4-year follow up for each period.

Data collection

Paper I and II

The data collection was conducted through interviews with the purpose to achieve rich informative data from men in Paper I and from women in Paper II.

In Paper I the interviews with the men (n=21) started in May 2011 and lasted until December 2012. The data analysis started simultaneously and continued until March 2013. According to Charmaz the data collection is not completed until the analysis of the data is assessed as saturated with no new insights during the comparisons of the theoretical categories.⁽⁸⁰⁾ All of the interviews except for one was performed in the CCU in a private room where the interviewer and the participant were undisturbed. One interview was conducted at the participant's home. The interviews were digitally recorded, lasted for 30-70 minutes and was performed by the first author (SN). All interviews were transcribed in verbatim and the first author (SN) transcribed 19 interviews and two were transcribed by a specialized company.

In Paper II the interviews with the women (n=17) started in June 2011 and lasted until May 2012. The interviews lasted for 25-140 minutes and were performed by the first author (AG). The interviews in this study were conducted at the women's home (n=10) at hospital before discharge (n=6) at hospital after discharge (n=1). Ten of the interviews were transcribed by the first author, one by the third author, six by a specialized company.

According to the grounded theory method, the data collection and analysis was conducted simultaneously.⁽⁸⁰⁾ The method enables a progress within the data collection with possibility to refine the interviews questions during each interview and during the study process. To start, the interviews were focused to explore the field in order to gain a wide range of experiences. Subsequently, this gives the researcher possibilities to develop the questions to become more specific. During the interview process it is essential to arrange an atmosphere where the participants feel comfortable to talk about their experiences.⁽⁸⁰⁾

All of the interviews began with a brief introduction where the participants were informed about the purpose with the study and asked whether they had any questions. To make the participants confident and willing to share their experiences the interviewer tried to establish a personal relationship if possible. All of the interviews started with asking questions about demographic data. This approach aimed to open up for an ease

of conversation. Thereafter, the interviews continued with open-ended questions: “can you please tell me how it all started when you had your heart attack”; “can you tell me how you felt, what you thought and what you did?” Follow up questions were asked to clarify details and to achieve deeper and broader information about the participants experiences and to go beneath the surface of an ordinary conversation. At the end of each interview, the participants were given the opportunity to ask questions or talk about something which was important for them in addition to the previous conversation. All of the men and women were offered a debriefing to talk about the emotions an interview might entail, but none of the participants expressed an interest in this offer.

Paper III and IV

Registries

Data collection in Paper III and IV was conducted through the use of the Swedish Inpatient Register (IPR) and the Cause of Death Register.

Diagnoses in the IPR are coded according to the Swedish International Classification of Diseases (ICD), which is based on the WHO classification system. The IPR was established in the 1960s and reached a complete national coverage in 1987. All hospitals are required to report discharge diagnoses to hospital admissions. The IPR register is considered to be suitable for large-scaled population based studies. The rate of missing diagnoses for somatic care is 0.8%. In general, positive predictive (PPV) values in the IPR register are 85-95% and in myocardial infarction it is 98-100%, with a sensitivity of about 77-91.5%.⁽⁸¹⁾ Another validation study by Hammar et al (2001) used the IPR to identify a subsample of patients with AMI (ICD-9 410) in the National Acute Myocardial Infarction Register, in whom the diagnosis was validated through medical records. In this study the PPV was 86% and with a sensitivity of 94%.⁽⁸²⁾

The registration of causes of deaths has a long tradition in Sweden. Sweden is following the International Statistical Classification of Diseases and Related Health Problems according to WHO since 1951. From an international perspective, the proportion of missing death certificates is fairly low in Sweden (0.8%), but with a tendency for an increasing trend in missing death certificates due to changed procedures in 1991.⁽⁸³⁾ According to a study by Johansson et al the validity for correct diagnosis in the causes of death register for ischemic heart disease (IHD) 1995 was 87%.⁽⁸⁴⁾ The validity varies according to age, with better validity for younger than older people. Causes of death among elderly people were more difficult to identify because they often suffer from several diseases.⁽⁸³⁾

Paper III

Identification of comorbidities was conducted by using the following main or contributory discharge codes during the preceding 7 years, including the index hospitalization: diabetes (ICD-8 and 9 250; ICD-10 E10–E14), hypertension (ICD-8 and 9 401–405; ICD-10 I10–I15), valvular disease (ICD-8 394–396, 424; ICD-9 394–397, 424; ICD-10 I05–I09, I34–I35), congenital heart disease (ICD-8 746–747; ICD-9 745–747;

ICD-10 Q20–Q26), stroke (ICD-8 and 9 431–434, 436; ICD-10 I61–I64), chronic respiratory disease (ICD-8 490-493; ICD-9 490–496; ICD-10 J40–J47), malignancy (ICD-8 and 9 140–208; ICD-10 C00–C97), renal failure (ICD-8 581, 583, 584; ICD-9 584-586; ICD-10 N17–N19), coronary artery bypass grafting (3067, 3066, 3105, 3127, FNA, FNB, FNE, FNC) and percutaneous coronary intervention (3080, FNG 00, FNG 02, FNG 05).

The following codes were used to examine causes of deaths among fatal cases: CVD (ICD-9 390-459; ICD-10 I00-I99), IHD (ICD-9 410-414; ICD-10 I20-I25), stroke (ICD-9 430-438; ICD-10 I60-I68) and all other causes (including malignancies (ICD-9 140-208; ICD-10 C00-C97). The all-cause mortality was estimated by a 4-year follow up for each of the four 5-year periods (1987-1991, 1992-1996, 1997-2001, 2002-2006).

Paper IV

Comorbidities were identified by using ICD system 8, 9 and 10, diabetes (ICD-8 and 9 250; ICD-10 E10–E14), hypertension (ICD-8 and 9 401–405; ICD-10 I10–I15), AMI (ICD-8 and 9 410; ICD-10-I21), valvular disease (ICD-8 394-396, 424; ICD-9 394–397, 424; ICD-10 I05–I09, I34–I35), congenital heart disease (ICD-8 746-747; ICD-9 745–747; ICD-10 Q20–Q26), heart failure (ICD-8 and 9 428; ICD-10 I50), atrial fibrillation (ICD-8 427.92; ICD-9 427D; ICD-10 I48), stroke (ICD-8 and 9 431–434, 436; ICD-10 I61–I64), chronic respiratory disease (ICD-8 490-493; ICD-9 490–496; ICD-10 J40–J47), renal failure (ICD-8 581, 583, 584; ICD-9 584–586; ICD-10 N17–N19), malignancy (ICD-8 and 9 140–208; ICD-10 C00–C97). ICD codes for diabetes, hypertension, valvular disease, congenital heart disease, chronic respiratory disease and renal insufficiency were defined by using discharge codes including the preceding 7 years before hospital admission for CABG. To avoid procedure related diagnoses, heart failure, atrial fibrillation, stroke and malignancy were defined by using ICD codes during the preceding 7 years until the day before admission to hospital for CABG. Variables from IPR register were utilized to define emergent and elective CABG procedures.

Data analysis

Paper I and II

Data collection and data analysis were performed simultaneously.^(80, 85) The analysis started immediately after the first interviews and was driven by the questions: what is happening here, and how do these statements affect the decision making process? The participants' expressed feelings, thoughts and actions linked to the decision making process which were noted and sorted into initial codes. The analysis was then undertaken to determine similarities, differences and patterns and from there to construct tentative categories. To refine and strengthen the tentative categories subsequent interviews were performed followed by additional constant comparisons between categories. This enabled the analysis to evolve into further levels of abstraction of the categories into theoretical concepts.^(80, 85)

Memo-writing was performed and involved in the data analysis in both Paper I and II. The memos consisted of written reflections connected to the interviews and theoretical influences from books and discussions with the research team.⁽⁸⁰⁾ Notes from the memo writing was then involved in the data analysis

Paper III and IV

The study populations in both Paper III and IV was divided into four periods (1987-1991; 1992-1996; 1997-2001; 2002-2006) with a four year follow up for each period.

The statistical analyses in Paper III and IV were performed with SAS 9.3, using R version 2.15.1 to obtain the graphs in Paper III. To estimate differences in baseline characteristics χ^2 test was used and t-tests to compare mean age within the respective age groups. Cochran Armitage to test for trend was used where a p-value of ≤ 0.05 was considered as significant.

Standardised Mortality ratio (SMR), Absolute risk (AR) and absolute excess risk (AER) were used in both Paper III and IV⁽⁸⁶⁾ to compare the mortality rate in patients with a first AMI and patients who underwent a first isolated CABG with those in the general population. The SMR was calculated as the ratio of the observed deaths in the study cohort to the expected number of deaths in the general population with 95% confidence intervals (CIs). To calculate the number of expected deaths, life expectancy tables by age, gender, and calendar year from Official Statistics of Sweden (SCB) were used

The AR for each period for the observed population was calculated by dividing the observed mortality with person-years and then multiplying by 100. In addition, to examine the additional mortality risk in the observed cohorts we estimated the AER. The AER calculations aimed to add a useful measure of annual average excess risk in absolute terms. This was estimated and defined as the absolute difference between observed and expected mortality among all patients. The calculation was performed by subtracting the expected number of deaths, from the number of observed deaths, divided by the number of person-years at risk and multiplying by 100.

Cox proportional hazard regression was used to estimate age and gender-specific changes in all-cause mortality over time.⁽⁸⁷⁾ The first period (1987–1991) was used as reference with a 95% CI for each period. The multivariable models in Paper III were adjusted for age, diabetes, hypertension, valvular and congenital heart disease, stroke, chronic respiratory disease, malignancy and renal failure. The multivariate models in Paper IV were adjusted for age, acute hospitalization, AMI, diabetes, hypertension, valvular, stroke, chronic respiratory disease, malignancy and renal failure. The models in Paper III and IV were also tested for proportionality assumption and interactions with time. In the final models only significant comorbidities and age were included

Survival probability was estimated in Paper III by using the Kaplan Meier method.⁽⁸⁸⁾ In addition, a log-rank test was conducted to study changes in survival between the time periods.

RESULTS

Paper I

The aim of this study was to describe actions and experiences involved in the process of seeking medical attention in men with a first AMI. In this study 21 men aged between 39 and 73 year attended. The decision making process appeared to be a complex and a nonlinear process with experiences and actions which either hindered or facilitated the men to seek medical care. The analysis resulted into three interconnected concepts appeared; bodily changes, maintaining daily life, and pursuing answers. Together these three concepts composed the core concept “cue to action” (Table 2).

Table 2. Overview for the concepts during men’s decision making process

| Bodily changes | Cue to action | |
|-----------------------|----------------------------------|-----------------------------|
| | Maintaining everyday life | Pursuing answers |
| Sensing the body | Stabilizing existence | Explaining discomfort |
| Adjusting to the body | Alleviating bodily discomforts | Confirming the suspicion |
| | Preserving the self | Being aware of the severity |

Experiencing bodily changes had a great influence on the men’s thoughts and actions during the decision process but also on the motivation to seek medical care. All the men experienced bodily changes of some kind, but the symptoms varied during the time before admission to hospital. Some men felt bodily changes several months before admission and others only the same day. There were varied descriptions of the symptoms from insidious symptoms to severe chest pain and the duration of the discomforts varied considerably.

During the process the men tried to maintain their everyday life. They struggled with how to act, preserving the hope that the symptoms would be harmless. They described great responsibility for their family, friends and colleague, not wishing to worry, scare or upset anyone with their illness experiences. To relieve the discomforts the men used different strategies such as medication for pain or stomach problem and some tried to rest, to eat or to have a drink of water. These actions helped in some cases for the moment but usually the relief was temporary and the discomfort would return.

One hindering factor for seeking medical care was a disposition to preserve an image of strength to other people including health professionals. Keeping up the self-image was regarded as a help to diminish the risk of being seen as weak or unmanly, providing a sense of control in their situation and preserving their integrity.

The men tried to structure and make sense of the experiences. When they compared their present and past experiences they could perceive variations and changes in symptoms, comparing with previous illness. This comparing started immediately after the first bodily changes and contributed to a decision to seek medical attention. Some of the men felt threatened and wanted some explanations for the discomfort that they felt.

The internet was used as a tool to obtain explanations of their bodily sensations but this often caused confusion since it was difficult to assess the wealth and heterogeneity of the information in relation to their own discomfort. They also used their preconceptions and prior knowledge about symptoms from AMI which they tried to compare with their own experiences. Vague or non-characteristic symptoms did not match their own conceptions of symptoms associated with an AMI. Instead the preconceptions of symptoms characteristic from an AMI consisted of strong chest pain and syncope. Vague and insidious symptoms was also associated as typical female symptoms of AMI. Some of the men contacted medical care providers but what they described was not perceived as an AMI, possibly due to lack of objective signs, such as changes in ECG or increased biomarkers for AMI. Such incidents made them hesitate to seek medical attention once again.

Prior to the decision to contact medical care the men compared all their experiences attempting to distinguish between of what was normal and abnormal. They felt threatened and wanted an explanation from healthcare professionals about their discomfort and they could not handle the situation on their own. An understanding of the abnormality in their situation, severity of condition or perceived illness experience was expressed solely or in combination which facilitated the decision to act

Paper II

The aim of this study was to identify how experiences of women with a first AMI interacted and influenced the decision to seek medical care. In total, 17 women between 38 to 75 years participated.

The core of the women's decision making process was a change in their view of their ability to carry on as normal, from a retrospective to a prospective perspective. This change was a construction of actions, thoughts and emotions which they experienced during the decision process. The decision-making process to seek medical care was divided into three levels sprung from symptoms as the driving forces; 1) Non-intriguing symptoms, 2) Symptoms interfering with normal activities, 3) Symptoms intruding on life. The concepts outlined a process where symptoms moved from being perceived as harmless to be alarming and were vertically dependent and horizontally following the qualitative leaps toward the decision to seek medical care. The symptoms was characterized by the women as recurring, insidious and suddenly accelerating (Figure 1).

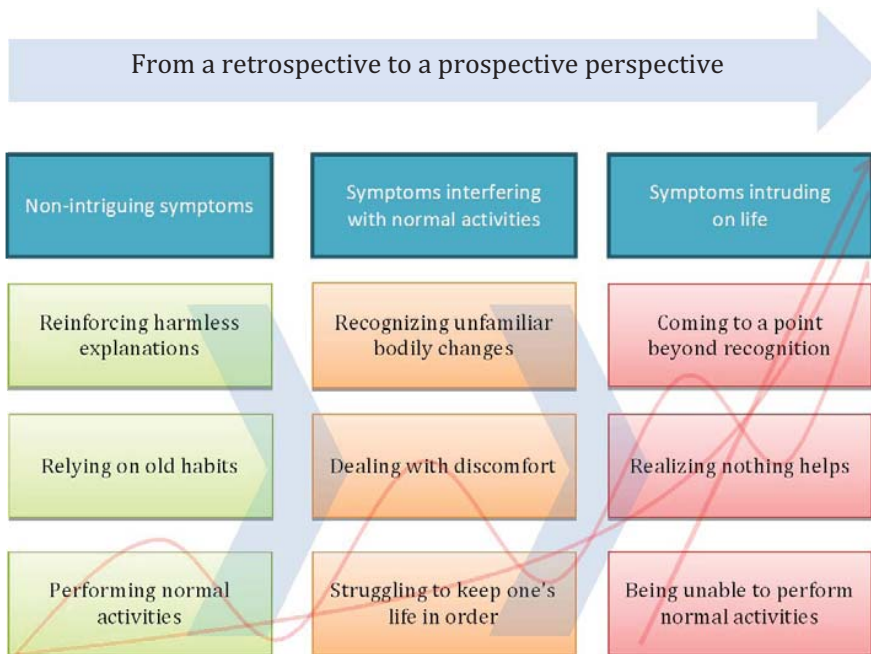


Figure 2. The progression of the decision-making process based on the interconnected concepts.

The result showed that harmless symptoms were associated to diagnoses that they had received earlier such as osteoarthritis, gastritis or other conditions. Insidious symptoms also contributed to attributing their symptoms to harmless conditions such as stress or muscle pain. The women relied on their own capabilities to handle the situation. Earlier successful management of symptoms or other previous health problems strengthened their perception of being someone who always had been able to manage situations. Recurring symptoms could cause an interruption in the daily activities but as soon as the symptoms disappeared they could complete their tasks. Intensified symptoms made the women aware of their bodies. They compared their present symptoms with previous experiences of illness. The location of the discomforts had a strong effect on the explanations of illness and in the assessment of the severity. However, the location of discomforts such as pain in the right arm were sometimes misleading. When the symptoms interfered with their daily activities they could no longer rely on what they use to do in similar instances and they had to deal with their new situation. The women found this difficult since they had a self-image of being independent of others, and had to struggle to carry on with their tasks.

Some women did seek medical care but their symptoms did not raise suspicion of AMI, which made them reluctant to seek care or advice again. Seeking medical care was a cause of additional stress because of the interruption in their daily life. Accelerating symptoms or intense symptoms caused difficulties to rely on previous expla-

nations and therefore caused feelings of fear or anxiety. The women started to reflect on what was most important in life and about the consequences of non-acting which strongly contributed to their final decision to seek medical care. When the symptoms intruded on their lives to the extent that normal activities or responsibilities could not be upheld the women realized the need of seeking medical care. In addition, realizing that they could do nothing to relieve the symptoms contributed to an understanding of the severity and brought them to a final decision.

Paper III

The aim of this study was to examine sex-specific trends in long-term survival in patients aged 25-54 years hospitalized with first AMI during 1987-2006, and to compare death rates with those of the general population separately for men and women. The study cohort consisted of 37,276 cases, 30,047 men and 7,229 women. Diabetes and hypertension were the most prevalent comorbidities in both men and women. However, women had more diabetes, hypertension, chronic lower respiratory disease and malignancies than men ($p < 0.0001$) (Table 3). Comorbidities in each four year period (1987-1991, 1992-1996, 1997-2001, 2002-2006) increased over time except for congenital heart diseases.

Table 3. Baseline characteristics in 37,276 men and women aged <55 years with a first AMI, 1987-2006

| | All | Men | Women | P-value |
|--|--------------|---------------|--------------|---------|
| Number of cases | 37 276 | 30 047 | 7 229 | |
| Age 25-44, n (%) | 7 905 (21.2) | 6 357 (21.2) | 1 548 (21.4) | |
| Mean age (SD) | | 40.21 (3.74) | 39.84 (4.04) | 0.055 |
| Age 44-54, n (%) | 29 371(78.8) | 23 690 (78.8) | 5 681 (78.6) | |
| Mean age (SD) | | 50.31 (2.75) | 50.39 (2.76) | 0.0549 |
| Diabetes, n (%) | 4 064 (10.9) | 3 017 (10.0) | 1 047 (14.5) | <0.0001 |
| Hypertension, n (%) | 4110 (11.0) | 3141 (10.6) | 969 (13.4) | <0.0001 |
| Valvular disease, n (%) | 287 (0.77) | 211 (0.70) | 76 (1.05) | 0.0023 |
| Congenital heart disease | 36 (0.10) | 23 (0.08) | 13 (0.18) | 0.0111 |
| Stroke, n (%) | 412 (1.11) | 302 (1.01) | 110 (1.52) | 0.0002 |
| Chronic lower respiratory disease, n (%) | 557(1.49) | 368 (1.22) | 189 (2.61) | <0.0001 |
| Malignancy, n (%) | 354 (0.95) | 255 (0.85) | 99 (1.37) | <0.0001 |
| Renal failure | 230 (0.62) | 164 (0.55) | 66 (0.91) | 0.0003 |
| CABG*, n (%) | 253 (0.68) | 221 (0.74) | 32 (0.44) | 0.007 |
| PCI*, n (%) | 235 (0.63) | 198 (0.66) | 37 (0.51) | 0.16 |

*Procedures dating at least 6 months prior to hospitalization for AMI. AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention

Men aged 25-44 year had a 4-fold risk of death compared to the general population in the last period while men aged 45-54 had a nearly 2-fold risk. Corresponding risk for death in women aged 25-44 showed a 14-fold risk and women aged 45-54 had a nearly six-fold risk compared to women in the same age in the general population (Table 4).

The annual excess risk of death decreased in men, regardless of age, during the study period. Women on the other hand showed a decrease in AER with a nadir value in the period 1997-2001 and then increasing in the last period (Table 4).

Multi-adjusted HR showed a decreasing mortality risk by 70% in men aged 25-44 and nearly as much in men aged 45-54. Among the youngest women the mortality risk decreased by 53% while in women aged 45-54 mortality improved by 47% (Table 4). Figure 3 shows an increased trend in survival during the four periods in men aged 25-54 years while corresponding estimates in women aged 25-54 years (Figure 4) showed an increased survival until the third period with a reverted trend in the last period to nearly that in the second period.

Table 4. Observed versus expected mortality ratio, estimated over 4 years, standardised mortality ratio, AR, absolute excess risk, and HR for mortality by age group and period among 37 276 men and women aged <55 years with a first AMI

| Age, Period | Observed* | Expected† | SMR (95% CI) | AR‡ | AER§ | HR (95% CI)¶ | HR (95% CI)** |
|--------------------|-----------|-----------|---------------------|------|------|------------------|------------------|
| Men 25-44 | | | | | | | |
| 1987-1991 | 113 | 16 | 6.88 (5.67–8.20) | 1.61 | 1.38 | 1.0 (ref) | 1.0 (ref) |
| 1992-1996 | 81 | 13 | 6.16 (4.89–7.57) | 1.25 | 1.05 | 0.76 (0.57–1.01) | 0.73 (0.55–0.98) |
| 1997-2001 | 58 | 10 | 5.70 (4.33–7.27) | 1.00 | 0.83 | 0.60 (0.43–0.82) | 0.53 (0.38–0.73) |
| 2002-2006 | 36 | 8 | 4.34 (3.04–5.87) | 0.65 | 0.50 | 0.41(0.28–0.60) | 0.30 (0.20–0.44) |
| Men 45-54 | | | | | | | |
| 1987-1991 | 465 | 125 | 3.72 (3.39–4.07) | 2.10 | 1.53 | 1.0 (ref) | 1.0 (ref) †† |
| 1992-1996 | 379 | 119 | 3.20 (2.88–3.53) | 1.56 | 1.07 | 0.74 (0.65–0.85) | 0.70 (0.61–0.81) |
| 1997-2001 | 289 | 108 | 2.69 (2.39–3.00) | 1.22 | 0.77 | 0.57 (0.49–0.66) | 0.50 (0.43–0.58) |
| 2002-2006 | 215 | 89 | 2.43 (2.12–2.76) | 0.99 | 0.59 | 0.47 (0.40–0.56) | 0.32 (0.27–0.39) |
| Women 25-44 | | | | | | | |
| 1987-1991 | 34 | 2 | 17.55 (12.15–23.94) | 2.39 | 2.26 | 1.0 (ref) | 1.0 (ref) |
| 1992-1996 | 28 | 2 | 17.99 (11.95–25.27) | 2.17 | 2.05 | 0.93 (0.56–1.55) | 0.85 (0.51–1.42) |
| 1997-2001 | 10 | 2 | 6.07 (2.89–10.42) | 0.63 | 0.52 | 0.27 (0.13–0.55) | 0.28 (0.14–0.56) |
| 2002-2006 | 21 | 2 | 13.53 (8.36–19.93) | 1.26 | 1.17 | 0.55 (0.32–0.94) | 0.47(0.27–0.83) |
| Women 45-54 | | | | | | | |
| 1987-1991 | 101 | 15 | 6.90 (5.62–8.31) | 2.25 | 1.93 | 1.0 (ref) | 1.0 (ref) # |
| 1992-1996 | 76 | 16 | 4.63 (3.65–5.73) | 1.45 | 1.14 | 0.64 (0.48–0.87) | 0.56 (0.42–0.76) |
| 1997-2001 | 68 | 19 | 3.58 (2.78–4.48) | 1.08 | 0.78 | 0.49 (0.36–0.66) | 0.44 (0.32–0.60) |
| 2002-2006 | 102 | 16 | 6.42 (5.24–7.73) | 1.72 | 1.45 | 0.77 (0.59–1.02) | 0.53 (0.39–0.71) |

*Observed number of deaths in the study population. †Expected number of deaths in the general population. ‡Absolute risk per 100 person-years. §Absolute excess risk per 100 person-years. ¶Age adjusted. **Multiadjusted for age, diabetes, hypertension, valvular, congenital heart disease, stroke, chronic respiratory disease, malignancy and renal failure. ††Adjusted for changes and interaction over time, malignancy, #chronic respiratory disease. AER, absolute excess risk AMI, acute myocardial infarction; AR, absolute risk; SMR, standardized mortality ratio; HR, hazard ratio; CI, confidence interval.

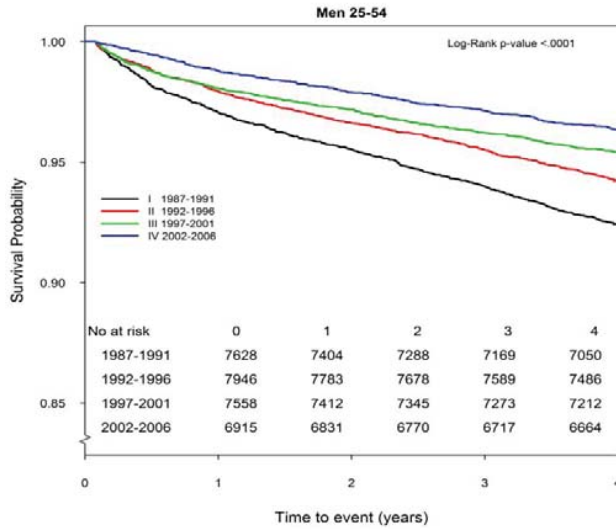


Figure 3. Four-year trend in survival probability by period and time among men (n 30 047) aged 25-54 years with a first acute myocardial infarction.

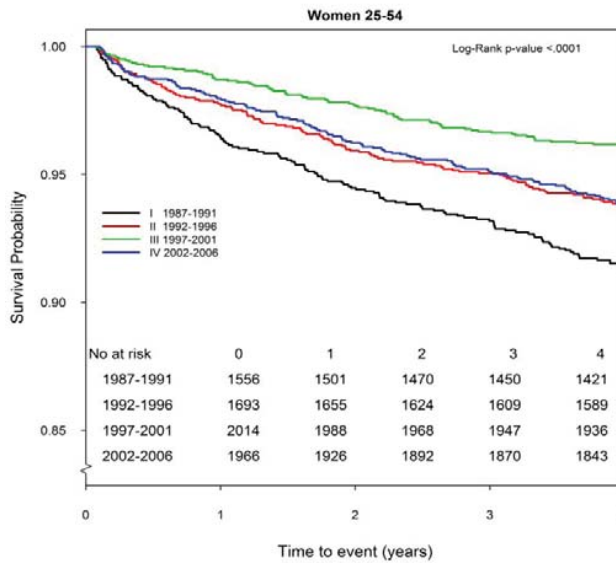


Figure 4. Four-year trend in survival probability by period and time among women (n 7229) aged 25-54 years with a first acute myocardial infarction.

Of the 2,076 deaths 1987-2006, deaths related to CVD decreased during the four five-years study periods from 78.6% to 55.4% in men and 58.5% to 34.1% in women (Table 5).

Table 5. Cause of death by period for 2076 deaths within 4 years among men and women aged <55 years with a first AMI during 1987–2006

| Cause of death | Total n (%) | Men n (%) | Women n (%) | p-value |
|-----------------------|------------------------|----------------------|------------------------|----------------|
| <i>1987-1991</i> | 713 | 578 (81.1) | 135 (18.9) | |
| CVD | 533(74.8) | 454(78.6) | 79 (58.5) | <0.0001 |
| IHD | 481 (67.5) | 405 (70.1) | 76 (56.3) | 0.0021 |
| Stroke | 18 (2.52) | 16(2.77) | 2 (1.48) | 0.3909 |
| All other causes | 180 (25.3) | 124 (21.5) | 56 (41.5) | <0.0001 |
| Malignancies | 55 (7.71) | 39 (6.75) | 16 (11.9) | 0.0454 |
| <i>1992-1996</i> | 564 | 460 (81.6) | 104 (18.4) | |
| CVD | 369 (65.4) | 318 (69.1) | 51 (49.0) | <0.0001 |
| IHD | 337 (59.8) | 295 (64.1) | 42 (40.4) | <0.0001 |
| Stroke | 6 (1.06) | 5 (1.09) | 1 (0.96) | 0.9104 |
| All other causes | 195 (34.6) | 142 (30.9) | 53 (51.0) | <0.0001 |
| Malignancies | 79 (14.01) | 57 (12.4) | 22 (21.2) | 0.0201 |
| <i>1997-2001</i> | 425 | 347 (81.7) | 78 (18.4) | |
| CVD | 242 (56.9) | 205 (59.1) | 37 (47.4) | 0.0606 |
| IHD | 216 (50.8) | 182 (52.5) | 34 (43.6) | 0.1573 |
| Stroke | 5 (1.18) | 3 (0.86) | 2 (2.56) | 0.2084 |
| All other causes | 183 (43.1) | 142 (40.9) | 41 (52.6) | 0.0606 |
| Malignancies | 63 (14.8) | 52(15.0) | 11 (14.1) | 0.8428 |
| <i>2002-2006</i> | 374 | 251 (67.1) | 123 (32.9) | |
| CVD | 181 (48.4) | 139 (55.4) | 42 (34.1) | 0.0001 |
| IHD | 145 (38.8) | 116 (46.2) | 29 (23.6) | <0.0001 |
| Stroke | 12 (3.21) | 7 (2.79) | 5 (4.07) | 0.5106 |
| All other causes | 193 (51.6) | 112 (44.6) | 81(65.9) | 0.00001 |
| Malignancies | 60 (16.0) | 28 (11.2) | 32 (26.0) | 0.0002 |

AMI, acute myocardial infarction; CVD, cardiovascular disease; IHD, ischaemic heart disease;

Paper IV

The aim of this study was to examine trends in 4-year survival among men and women after a first isolated CABG during 1987-2006 and to compare the mortality rates to those of the general population. In this population based study we identified 96,254 patients, of these, 1,310 men and 616 women died during the first 30 days. Of the remaining 94,328 patients who survived 30 days 74,113 (78.7%) were men and 20,215 (21.4%) were women.

During the study period (1987-2006) there was an observed overall higher proportion of most comorbidities in men aged ≥ 55 compared to men aged 18-54 years. Women aged ≥ 55 had more comorbidities than women aged 18-54 years, except for diabetes and renal insufficiency (Table 6).

In the last period (2002-2006) younger men (<55 years) had a nearly two-fold risk for mortality compared to the men of the same age in the general population. Corresponding mortality rates for women showed a nearly four-fold mortality risk. However, in both men and women aged ≥ 55 years the standardised mortality risk was lower than for the general population with an annual excess mortality risk of -0.85 in men and women -0.46 in the last period (Table 7).

When we included the first 30 day postoperative period the mortality risk remained lower than in men in the general population for men 55 years and older. However, women in the same age group showed an increased mortality risk with a SMR of 1.12 (95% CI, 1.03-1.22).

There were no significant changes in mortality risk in the unadjusted models for mortality risk among 30 days survivors during the study period. However, the adjusted models showed a continuously decreasing trend in mortality by 31% (HR 0.69 95% CI, 0.63-0.76) in men aged ≥ 55 years and by 37% (HR 0.63 95% CI, 0.46-0.88) in men aged <55 years. Corresponding HRs for women aged ≥ 55 years showed a decreasing trend by 38% (HR: 0.62 95% CI, 0.52-0.75) while younger women (<55 years) did not display any significant difference in the adjusted HR during the study period (HR: 1.02, 95% CI, 0.52-2.03) (Table 7).

Table 6. Baseline characteristics for 94,328 women and men age with a first isolated CABG in Sweden 1987-2006 by sex and age, surviving the 30 first days after CABG

| | Men All n (%) | Men 18-54 n (%) | Men ≥55 n (%) | P-value | Women All n (%) | Women 18-54 n (%) | Women ≥55 n (%) | P-value |
|-----------------------------|---------------------|-----------------------|---------------------|---------|-----------------------|-------------------------|-----------------------|---------|
| Number of patients | 74113 (78.7) | 11859 (16.0) | 62254 (84.0) | | 20215 (21.4) | 2145 (10.6) | 18070 (89.4) | |
| Mean age (SD) | 64.2 (9.3) | 49.2 (4.4) | 67.1 (6.9) | | 66.8 (9.1) | 48.7 (4.9) | 69.0 (6.8) | |
| AMI | 34223 (46.2) | 5642 (47.6) | 28581 (45.9) | 0.0009 | 9584 (47.4) | 901 (42.0) | 8683 (48.1) | <.0001 |
| Acute hospitalization | 20530 (27.7) | 3617 (30.5) | 16913 (27.2) | <.0001 | 5768 (28.3) | 650 (30.3) | 5118 (28.3) | 0.055 |
| Diabetes | 10775 (14.5) | 1611 (13.6) | 9164 (14.7) | 0.0013 | 4136 (20.5) | 557 (26.0) | 3579 (19.8) | <.0001 |
| Hypertension | 15186 (20.5) | 2085 (17.6) | 13101 (21.0) | <.0001 | 5865 (29.0) | 491 (22.9) | 5374 (29.7) | <.0001 |
| Heart failure | 6333 (8.55) | 556 (4.69) | 5777 (9.28) | <.0001 | 2240 (11.1) | 141 (6.57) | 2099 (11.6) | <.0001 |
| Atrial fibrillation | 3357 (4.53) | 138 (1.16) | 3219 (5.17) | <.0001 | 857 (4.24) | 16 (0.75) | 841 (4.65) | <.0001 |
| Valvular disease | 1508 (2.03) | 90 (0.76) | 1418 (2.28) | <.0001 | 679 (3.36) | 23 (1.07) | 656 (3.63) | <.0001 |
| Congenital heart disease | 57(0.08) | 7 (0.06) | 50 (0.08) | 0.4434 | 12 (0.06) | 2 (0.09) | 10 (0.06) | 0.4957 |
| Stroke | 1309 (1.77) | 108 (0.91) | 1201 (1.93) | <.0001 | 345 (1.71) | 23 (1.07) | 322 (1.78) | 0.0164 |
| Chronic respiratory disease | 2204 (3.00) | 177 (1.49) | 2027 (3.26) | <.0001 | 845 (4.18) | 58 (2.70) | 787 (4.36) | 0.0003 |
| Renal insufficiency | 829 (1.10) | 105 (0.89) | 724 (1.16) | 0.0084 | 212 (1.05) | 42 (1.96) | 170 (0.94) | <.0001 |
| Malignancy | 1356 (1.83) | 103 (0.87) | 1253 (2.01) | <.0001 | 333 (1.65) | 21 (0.98) | 312 (1.73) | 0.0101 |

Table 7. Four year standardised mortality ratio (SMR), absolute risk (AR), absolute excess risk (AER) and hazard ratio (HR) by age groups and period in men and women who underwent first CABG, surviving the 30 first days after CABG.

| Sex, Age Period | Observed deaths (n) | Expected deaths (n) | SMR(95% CI) | AR %* | AER % † | HR | Multi adjusted HR |
|--------------------|---------------------|---------------------|------------------|-------|---------|------------------|-------------------|
| <i>Men 18-54</i> | | | | | | | |
| 1987-1991 | 109 | 63 | 1.74 (1.43-2.08) | 0.98 | 0.41 | 1.0 (ref) | 1.0 (ref) ‡ |
| 1992-1996 | 119 | 76 | 1.56 (1.30-1.86) | 0.81 | 0.29 | 0.82 (0.64-1.07) | 0.76 (0.60-1.01) |
| 1997-2001 | 82 | 59 | 1.39 (1.11-1.71) | 0.66 | 0.18 | 0.67 (0.51-0.90) | 0.57 (0.43-0.77) |
| 2002-2006 | 63 | 36 | 1.76 (1.35-2.22) | 0.76 | 0.33 | 0.78 (0.57-1.06) | 0.63 (0.46-0.88) |
| <i>Men ≥55</i> | | | | | | | |
| 1987-1991 | 820 | 1063 | 0.77 (0.72-0.83) | 2.14 | -0.63 | 1.0 (ref) | 1.0 (ref) § |
| 1992-1996 | 1653 | 2295 | 0.72 (0.69-0.76) | 2.35 | -0.91 | 1.10 (1.01-1.20) | 0.88 (0.81-0.96) |
| 1997-2001 | 1564 | 2368 | 0.66 (0.63-0.69) | 2.23 | -1.14 | 1.04 (0.96-1.13) | 0.76 (0.69-0.83) |
| 2002-2006 | 1428 | 1937 | 0.74 (0.70-0.78) | 2.39 | -0.85 | 1.12 (1.03-1.22) | 0.69 (0.63-0.76) |
| <i>Women 18-54</i> | | | | | | | |
| 1987-1991 | 16 | 6 | 2.72 (1.55-4.22) | 0.87 | 0.55 | 1.0 (ref) | 1.0 (ref) |
| 1992-1996 | 24 | 8 | 3.18 (2.03-4.58) | 0.99 | 0.68 | 1.14 (0.61-2.14) | 1.07 (0.57-2.02) |
| 1997-2001 | 21 | 8 | 2.70 (1.67-3.98) | 0.82 | 0.52 | 0.94 (0.49-1.81) | 0.75 (0.38-1.46) |
| 2002-2006 | 20 | 4 | 4.49 (2.74-6.68) | 1.23 | 0.95 | 1.41 (0.73-2.72) | 1.02 (0.52-2.03) |
| <i>Women ≥55</i> | | | | | | | |
| 1987-1991 | 192 | 157 | 1.22 (1.05-1.40) | 2.09 | 0.38 | 1.0 (ref) | 1.0 (ref) # |
| 1992-1996 | 428 | 457 | 0.94 (0.85-1.03) | 2.09 | -0.14 | 1.00 (0.84-1.19) | 0.77 (0.65-0.92) |
| 1997-2001 | 442 | 564 | 0.78 (0.71-0.86) | 2.01 | -0.55 | 0.96 (0.81-1.14) | 0.66 (0.57-0.80) |
| 2002-2006 | 380 | 461 | 0.82 (0.74-0.91) | 2.15 | -0.46 | 1.03 (0.87-1.22) | 0.62 (0.52-0.75) |

*AR, Absolute risk per 100 person-year. †AER, Absolute excess risk per 100 person-year. ‡Men 18-54 multi adjusted for age, acute hospitalization and significant comorbidities (myocardial infarction, heart failure, valvular disease and renal failure). §Men ≥55 multi adjusted for age, acute hospitalization and significant comorbidities (myocardial infarction, diabetes, heart failure, atrial fibrillation, valvular failure, chronic respiratory disease, renal failure, and malignancy). ||Women 18-54; multi adjusted for age, acute hospitalization and significant comorbidities (diabetes). #Women ≥55; Multi adjusted for age, acute hospitalization and significant comorbidities (myocardial infarction, diabetes, heart failure and chronic respiratory disease and renal failure)

DISCUSSION

Paper I and II

Symptoms as the driving force in the decision process

The main findings in Paper I and II are that the decision process is complex. Irrespective of gender, the broad spectra of symptoms with subsequent interpretations had a great impact on the decision process.

Both men and women experienced varied symptoms from vague and insidious to intense pain, from several months before admission to days before. These experiences of prodromal symptoms are described in previous studies.^(25, 58, 89, 90) Vague and intermittent symptoms were difficult to assess which increased the uncertainty whether to contact medical care. As in previous studies,^(15, 58, 91) both men and women tried to relieve the symptoms on their own instead of seeking medical care. Knowledge about prodromal symptoms as a predictor of future AMI is not sufficient. Future research must gain a deeper understanding of the symptom patterns and characteristics in both men and women separately because of gender differences. Moreover, men did not interpret vague or insidious symptoms as AMI believing symptoms were supposed to be dramatic or more typical with intense chest pain, pain in the left arm and syncope. The women had difficulties to distinguish between normal bodily discomfort and the new symptoms. Regardless of how the symptoms were interpreted they caused a delay in the decision to seek medical care in both men and women. Difficulties in interpreting initial symptoms were also described in earlier studies.^(24, 53, 58, 91, 92) The men's preconceptions about gender differences in symptoms where vague and insidious symptoms was associated with symptoms in women are indeed important to further investigate within the delay concept because of the clinical implications.

Some studies show that chest pain is the most common symptom in both men and women.^(17, 18) However, some studies have reported higher frequencies of chest pain in men than in women.^(14, 20, 93) Women are reported to present more pain radiating to the back or throat, nausea, vomiting and palpitations.^(18, 94, 95) Previous studies have also found that older patients had more atypical symptoms and more rarely present with chest pain.⁽⁹³⁾ Despite differences in symptom presentation, it is important to remember that symptoms from other parts of the body are common in both men and women. It is crucial to increase this knowledge among health care professionals as well as the general public.

Several men and women sought medical care for their symptoms but did not receive an initial AMI diagnosis. Instead they were not diagnosed at all or, in some cases, the symptoms were attributed to stomach problems. Lack of objective signs might be one explanation to this. However, this caused hesitation to seek medical care once again and moreover the persons became lulled into a false security. In addition, some of the men felt ignored and some women did also describe a sense of reduction of their own

capacity to perceive illness perception. This result indicates that there is need for an improved dialogue between health care professionals and patients'. The patient's experiences of their discomfort must be integrated in the diagnostic process. Our result showed that subjective experiences are subordinated objective signs of disease in the contact with health care professionals. The discrepancy between illness as a subjective experience and disease as an objective dysfunction is known.^(96, 97) Absence of attentive listening or being ignored as an equal person contributes to increase the feeling of being dismissed.⁽⁹⁸⁾ It can also cause reluctance to ask important questions and worries about being a troublesome person.⁽⁹⁹⁾ In the continuous work with reducing delay in time from initial symptoms to treatment of AMI the skills to listen and bring an informative dialogue is essential to consider for health care professionals. Future research should also include interventions aimed to evaluate the improvement of the dialogue between health care professionals and the patients especially when patients seek medical attention for vague and insidious symptoms.

A previous unreported finding among the men, but not among the women was the use of the internet as a tool to obtain information about insidious and vague symptoms but the patients also reported difficulties in interpreting all the information. This finding indicates the complexity and difficulty for lay people to interpret health information on Internet. However, it is likely that the internet will become more common in both men and women as a source for health information. In the future the internet could be a useful source of information for AMI patients in the efforts to reduce delay in time.⁽¹⁰⁰⁾ However, a major challenge seems to be how information about symptoms for AMI should be presented at web pages. The findings from our study show that it is critical that the contents at webpages are adapted to how in how lay people interpret health information and further research is therefore needed about how to design this information

Emotional responses to symptoms

Both men and women were anxious not to seek medical care unnecessarily. It is possible that some of this reluctance was grounded in social constructions. The men were worried to be seen as weak or unmanly and wanted to uphold an image of being strong in front of others and themselves. Some of the men referred these beliefs to a socialization evolving an expectation to be strong. Similar findings are also described in previous studies.⁽¹⁰¹⁻¹⁰³⁾ Despite the fact that they suspected that they had a serious condition some did not seek medical care because of the risk to be perceived as a weak person. Women on the other hand describe that they were worried about their independency, with the risk of not being able to deal with their responsibilities at home or at work. Previous studies have also reported that concerns and responsibilities for others cause hesitation to seek medical care.^(104, 105) Moreover, there were also concerns among the women that an admission to hospital would cause a transformation from an independent and meaningful individual to an anonymous nobody. This was something that sometimes prolonged the decision process. Accordingly, it is indeed important that the health care professionals are aware of the concerns expressed by the men and women.

It is not possible to state that the results from Paper I and II reveal female or male barriers into health care seeking since this was not the initial focus. However, Galdas et al (2010) tried to explore the impact of gender among patients who had symptoms from an acute cardiac event.⁶⁰ Concordant with our study, some of the participant men fitted into the stereotypic pattern as stoic and strong while being responsible for the welfare of others was expressed by women. Still, men and women's behavior could not be fitted into distinct gender patterns since stereotypical masculine and feminine behaviors were seen in both men and women.

Whether hesitation to contact medical care is grounded in a specific gender construction or not is something that health care professionals must strongly consider in the dialogue when gathering information. Irrespective of gender, it is important to be aware of patients' behaviors and thoughts. However, it is also of interest to investigate further how health care professional's beliefs about gender differences may affect the diagnostic process. A majority of all death caused by coronary disease occur outside hospital.⁽³⁷⁾ It is possible, but not proven, that these individuals had prodromal symptoms or contacted medical care for bodily discomforts before death. Accordingly, death outside hospital could be a result of an unnecessarily delayed decision process. The responsibility to act in these circumstances rests with the person involved but in order to avoid unnecessary deaths a greater responsibility must be taken by the health care system with correct information to the lay public, ease of access to care and the skills to be receptive to the patients experiences.

Paper III

We found that the 4-year prognosis has improved among younger men and women (<55 years) surviving the 28 first days after a first AMI during the years 1987-2006. There are a limited number of studies in long term outcomes for prognosis in younger patients. However, a previous study from Sweden⁽¹⁰⁶⁾ showed that patients younger than 46 years old with STEMI had an annual mortality around 1% regardless of gender which is similar to the results of our study and to prior publications from our group.⁽¹⁰⁷⁾ The annual mortality increased with age and is about 6% for those aged 65-74 years and more than 12% among patients aged 75-84 years.⁽¹⁰⁷⁾ These figures are a vast improvement to prior estimates from the prethrombolytic era where the annual death rates after one year was 5% regardless of age.⁽¹⁰⁸⁾ Further, the annual mortality in the late 1980s was about 2% in younger patients.⁽¹⁰⁷⁾

There are several reasons for the improved survival. Some of the factors can be due to the development in pharmacological treatments and invasive revascularization techniques. Guidelines for management have been developed in connection with increased evidence from research and technical advances.^(12, 61, 109) It is also reported that PCI and evidence-based medical treatment is more common among individuals aged <55 year old than in elderly patients.⁽¹¹⁰⁾ Further, some of the decreasing trend can be due to more sensitive biochemical methods together with changes in criteria for diagnosis^(109, 111) which may contribute to less severe AMIs being detected and diagnosed. Accordingly, some of the improvement could be attributed to technical circumstances

Moreover, previous studies have also showed that the clinical presentation in patients with AMI has changed, with less severe infarctions and STEMIs.^(34, 112) It is known that smoking is associated with a higher risk of developing STEMI rather than non-STEMI.⁽³⁴⁾ Smoking rates have declined since 1980 and could contribute to explain the decreasing trend. However, this declining trend has stalled in the most recent years.⁽¹¹³⁾ If this stagnation in smoking trends among younger people will result in more severe infarctions will be important to monitor in future studies. There is also improvement in secondary prevention with an increased proportion of patients who receive antihypertensive, antiplatelet and lipid medication since the start of reporting to the national quality register in 1995.⁽⁷²⁾

Improvements in reporting diagnosis due to financial incitements can be an explanation to the increased trend in comorbidities.⁽⁸¹⁾ During the study period we observed an increased trend in hypertension this can also partly be explained by changes in criteria for hypertension and guideline management.⁽¹¹⁴⁾

Among the youngest women (aged 25-44 years) the absolute mortality rate was favorable until the last period (2002-2006) but then reverted to the same level as in the third period (1997-2001). This is challenging to explain but could reflect a limited number of cases during this period. Moreover, changes in more sensitive biomarkers during this period may have an impact and could be stronger in women than in men. Luepker et al observed an increased rate of AMI by 64% in men and 95% in women, when measuring simultaneously creatinine kinase MB and troponin.⁽²⁸⁾ Since increased troponin levels can reveal other diseases it can reflect an increased morbidity in other diseases than AMI.⁽¹¹⁵⁾ This is supported by the results in our study of the observed increasing trend in comorbidities and a decreasing trends in deaths caused by CVD.

Few studies have compared the mortality among young individuals with a first AMI to those in the general population. We found that the risk of mortality in men compared to the general population were between 2 to 4 fold higher in the last period 2002-2006. Corresponding mortality risk for women varied from 6 to 13 fold higher risk than women in the same age in the general population. A study by Smolina⁽¹¹⁶⁾ found that 387452 individuals surviving from an AMI the first 30 days between 2004 and 2010 had a 2 fold higher risk for mortality compared to the population. The risk was highest among the youngest population (<55 years) with about 2 fold higher in men and 6 fold higher in women which is similar to our study (K.Smolina personal communication). In our study, the youngest women showed a SMR of 13.5 (95% CI, 8.36-19.93) in our study. This result may reflect the small number of expected deaths among women in the general population, but will have to be followed in future studies.

Paper IV

In Paper IV we observed an overall improved survival in men and women aged ≥ 55 years old who survived the first 30 days after a first isolated CABG, after adjustments for comorbidities. However, in younger women (<55 years) there were no significant improvements.

Our study was carried out during a period where the technical development improved rapidly. Moreover, increased knowledge about revascularization procedures has formed a basis for the development of guidelines for myocardial revascularization procedures.⁽⁶⁷⁾ This has contributed to a more individualized preoperative selection and is a likely explanation for the observed improved survival in our study. As a result of the introduction and development of PCI, which has become the primary revascularization method in AMI patients, a significantly declining trend in the proportion of acute procedures was observed. However, there is also a possibility that patients with a high preoperative profile risk become deselected from CABG surgery at an early stage of the decision process (before presented to the surgeons) which could have an effect on the favorable trends.

As in previous studies we observed an overall increasing trend in comorbidities but this seems not to have influenced the mortality in our study among men or women ≥ 55 years. Furthermore, it is reported that patients with high preoperative risk receive benefits from CABG surgery.^(117, 118) Another explanation for the favorable trends in outcome in our study could be due to improvements in risk factors in the population and improved medication in primary prevention with better treatment of risk factors for the development of coronary heart disease.⁽³⁸⁾

In addition, secondary prevention after acute myocardial infarction has also improved with an increased proportion of patients receiving lipid-lowering drugs, ACE inhibitors, beta-blockers and antiplatelet medication.^(72, 119)

Women < 55 years surviving the first 30 days after surgery did not show any significant improvement in survival. Possible explanations can be the significantly increased trend in comorbidities as diabetes, hypertension, heart failure, renal insufficiency and stroke. Risk factors as smoking, hypertension, diabetes and high levels of low-density lipoprotein (LDL) have a greater association with myocardial infarction in younger women (< 60 year) than in older women (> 60 year).⁽³²⁾

It also is reported that women with diabetes and myocardial infarction have a substantial cardiovascular risk burden and higher risk of presenting with more severe infarctions (STEMI) and in-hospital mortality.^(120, 121) The proportion of diabetes increased from 19.5% (1987) to 36.1% (2006) in these younger women and may be one reason for lack of improved survival. Even so, previous studies have shown that patients with diabetes and three-vessel disease have more benefit from CABG surgery than PCI.⁽¹²²⁾ Moreover, women presenting with CHD about five to ten years later than men⁽³²⁾ which can be attributable to hormonal protection.^(123, 124) It is possible that the young women in our study have lost their advantages of hormonal protection because of high proportion of risk factors for coronary heart disease and that this effect persists after CABG surgery.

Previous studies have also found higher mortality in women after CABG.^(76, 125, 126) Less extensive revascularization with fewer distal anastomoses, fewer arterial grafts, smaller body surface and coronary arteries are some possible explanations to wom-

en's disadvantages in survival after CABG.^(77, 127, 128) Future studies are warranted to identify which factors influence the prognosis in women. More detailed data about variables such as smoking, diabetes, hypertension, metabolic aberrations and medication is important to consider and may contribute to increased knowledge of younger women's disadvantages after CABG surgery.

Our study showed that men and women ≥ 55 years who survived 30 days after CABG surgery had a markedly favorable outcome with lower mortality rates and reduced excess risk compared to those in the general population. The favorable outcome in our study can also be attributed to the still high risk of death in CHD in the general population where the majority of all death occurs out of hospital.⁽³⁷⁾ In contrast to this, the CABG population is detected in time and receives treatment for a progressive and life-threatening disease.

Few other studies have compared the mortality risk among CABG patients to the general population. However, a Finish study found that the mortality risk for men aged 35-64 years was similar to that of the general population while women had a 2 fold higher risk.⁽¹²⁹⁾ Another study by Stähle et al (1994) concluded that the survival among patients who underwent CABG surgery in 1970 to 1989 was nearly equal to the general population s but with an increased mortality after 6 to 8 years.⁽¹³⁰⁾ The results from the present study may be a marker of treatment benefits among men and women ≥ 55 years in a four year follow up. However, other studies confirm the reduced benefit with time after CABG surgery. In 10 years after surgery, new lesions was found in a majority of saphenous grafts and in the native vessels.⁽¹³¹⁾ Another study with a 30 year follow up showed that a majority (94%) needed repeated interventions with either PCI or CABG.⁽¹³²⁾

Strengths and limitations

Paper I and II

The interviews with 21 men and 17 women generated rich data with a wide variety of experiences and actions during their decision process. There was a wide range in ages which means that our findings are likely transferable to men and women of all ages. The interviews were conducted within 2 weeks after hospitalization to minimize recall bias. Since a majority of all fatal events of CHD occur out of hospital, it is not possible to guarantee that the results are transferable to the men and women with acute coronary events in general. However, some persons dying outside hospital also in all probability experienced some hesitation to seek medical care, maybe even to a greater extent than the men and women in our study. To strengthen the credibility of the results in both Paper I and II meetings were held continuously with all the authors to refine and discuss the codes and categories.

Paper III and IV

The main strengths in both Paper III and IV includes the nationwide coverage with virtually no loss to follow-up and the large sample size. One of the limitations in both

Paper III and IV is the reliance on the IPR. This register does not provide clinical variables such as blood chemistry, electrocardiographic findings, left ventricular function, medication, smoking, ethnicity or socioeconomic status and other detailed clinical information. Moreover, the diagnostic codes in Paper III and VI and codes for surgery in Paper IV were not uniform during the study period. This might contribute to an underestimation of comorbidities in the first years. The quality of the data is obviously of fundamental importance and validation studies of the IPR indicate a reasonable validity for myocardial infarction⁽⁸¹⁾ and of other major diagnoses.

In Paper III and IV the cause of death register was also used. Even though incorrect death certificates can lead to uncertainty in validity, CHD diagnoses have been estimated to be correct in 87%.⁽⁸⁴⁾ However, a correct diagnosis of death is likely more reliable for younger people than in the elderly.⁽⁸³⁾

CONCLUSIONS

Both men and women express a variety of intermittent, vague and insidious symptoms before admission to hospital. These bodily discomforts did not correspond with their preconceptions about AMI symptoms and prolonged the decision process.

Our finding shows that experiences of vague and insidious symptoms of an AMI are subordinated objective signs in men and women. This indicates that there is scope for an improved dialogue between health care professional and individuals.

There was a favorable trend in survival for men and women below 55 years old surviving their first AMI between the years 1987 and 2006. The risk of mortality decreased by 70% in men and by approximately 50% in women

Men <55 years surviving a first AMI (1987-2006) showed a 2- to 4 fold increased mortality risk compared to men in the general population. Corresponding risk for women ranged from a 6 fold risk to a nearly 14 fold risk.

Men and women ≥ 55 years surviving the first 30 days after CABG showed a lower mortality risk than those to the same age in the general population while equivalent risks for men and women <55 years was nearly 2 fold higher in men and nearly 5 fold in women.

After considering rising comorbidities there was a significant improvement in survival for all men and women surviving the first 30 days after CABG surgery except for women below 55 years of age.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Hjärt- och kärlsjukdomar är den vanligaste dödsorsaken i Sverige och stora delar av världen. Under de senaste 30 åren har framförallt dödlighet i hjärtinfarkt men även incidens minskat dramatiskt. Trots denna positiva utveckling insjuknar fortfarande en stor grupp individer i hjärtinfarkt varje år. Det övergripande syftet med denna avhandling var att studera män och kvinnors erfarenheter, strategier och handlingar i samband med symtom vid en första hjärtinfarkt samt att studera trender och prognos i överlevnad hos individer med kranskärlssjukdom.

I delstudie I och II genomfördes intervjuer med 21 män och 17 kvinnor som genomgått en första hjärtinfarkt. I delstudie III identifierades 37 276 män och kvinnor under 55 år som genomgått en första hjärtinfarkt från patientregistret. I delstudie IV identifierades 94 328 män och kvinnor som genomgått en kranskärlsoperation från patientregistret. Dödsorsaksregistret användes i både studie III och IV.

Resultaten från studie I och II visade att både män och kvinnor upplever en stor variation av symtom tiden innan sin diagnos för hjärtinfarkt. Vaga och återkommande symtom förekom och dessa förknippades inte med typiska symtom för akut hjärtinfarkt. Männerna hade en föreställning att hjärtinfarkt innebar kraftig bröstsmärta, smärta i vänster arm och svimning. Kvinnorna beskrev att de hade svårt att urskilja sina vaga symtom från tidigare fysiska besvär och prioriterade ansvaret för olika aktiviteter i det dagliga livet före sin hälsa. När männen jämförde tidigare erfarenheter med sin nuvarande situation kunde allvaret förstås i situationen eller att det inte var möjligt att hantera situationen på egen hand vilket bidrog till att man sökte vård. Tilltagande besvär hos kvinnorna orsakade problem med att utföra sina dagliga åtaganden, tidigare förklaringar kunde inte heller vidmakthållas vilket bidrog till en förståelse för att man behövde söka vård. Det fanns både män och kvinnor som sökte vård för vaga symptom tiden innan sin diagnos för hjärtinfarkt men då de inte uppvisade några objektiva tecken på hjärtinfarkt fick de antingen ingen diagnos alls, eller andra diagnosers om text magbesvär. Detta skapade en falsk säkerhet men också en känsla av att bli avfärdad samt minskad tilltro till den egna förmågan att tolka kroppens signaler, vilket bidrog till tveksamhet att söka vård återigen.

Resultat från delstudie III visade att män yngre än 55 år, som haft en första hjärtinfarkt mellan åren 1987 till 2006, i den sista studieperioden (2002-2006) hade en ca 2 till 4 gånger högre risk för död jämfört med män i samma ålder i befolkningen i övrigt. För kvinnor i motsvarande period och ålder fann man en 6 till 14 gånger högre risk för död. Prognosen i överlevnad 4 år efter en hjärtinfarkt visar en stabil förbättring hos männen sett över hela studieperioden (1987-2006). Även hos kvinnor kunde en förbättrad prognos i överlevnad observeras fram till den sista perioden (2002-2006) dock var överlevanden ungefär i samma nivå som vid andra perioden (1992-1996).

Delstudie IV visade att män och kvinnor över 55 år som genomgått en första kranskärlsoperation hade en lägre risk för död än män och kvinnor i samma ålder i befolk-

ningen. Totalt sett över hela studieperioden kunde en förbättrad prognos för överlevnad 4 år efter operationen observeras för dem som var över 55 år. Kvinnor yngre än 55 år hade en 4 gånger högre risk för död jämfört med kvinnor i befolkningen under den sista studieperioden (2002-2006). Överlevnaden 4 år efter en kranskärlsoperation hos dessa yngre kvinnor var oförändrad från första till sista studieperioden. Yngre män hade en ca 2 gånger högre risk för död jämfört med män i samma ålder som inte genomgått kranskärlskirurgi.

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