Unexplained chest pain in men and women

- symptom perception and outcome

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To Susanna Charlotta Beata

ABSTRACT

Patients with chest pain account for a large number of all patients seeking health care. The majority of these patients are referred to emergency departments (ED) and many of them are given a discharge diagnosis of unexplained chest pain (UCP). Our knowledge of this increasing number of patients with UCP is limited. The overall aim of the thesis was to describe and analyse symptom perception, psychosocial factors, health-related quality of life (HRQOL) and outcome of unexplained chest pain (UCP) in men and women.

The UCP patients' symptoms and their influence on daily life in a gender perspective were explored in Paper I using open interview questions (11 men and 9 women). A cross-sectional design was used in Paper II, assessing pain characteristics using the Pain-O-Meter and measuring psychosocial factors and HRQOL with a self-administered questionnaire. The results were based on 101 men and 78 women consecutively admitted to an ED. In Paper III, psychosocial factors and HRQOL were compared between the UCP patients (127 men and 104 women) and a reference group, i.e. a subsample (490 men and 579 women) from the INTERGENE population study. Paper IV was a register study with data from the Swedish National Hospital Discharge Register, investigating trends in incidence and outcome among patients hospitalised with UCP, angina pectoris or acute myocardial infarction (AMI) in Sweden in 1987-2003 (n=559 879).

The results showed that the men and women with UCP are generally middle-aged. More than a third of both UCP men and women were born outside Sweden and, compared with the reference group, the percentage of immigrants was significantly higher. UCP impacted negatively on the patients' daily life, which was filled with worries due to the chest pain. Feelings of panic and fear of death in connection with the chest pain were reported. Words like "pressure" and "cramp" were used when describing the chest pain, with few gender differences. Significant correlations were found between pain intensity and smoking in men (p < 0.01) and between pain intensity and age in women (p < 0.05). Chest pain intensity was not significantly associated with the UCP patients' reported HRQOL, apart from physical functioning in men (p < 0.05), but it was rated lower than the reference group of both UCP men and women. The UCP men in particular reported stress at work. The women with UCP presented more depressive symptoms and more symptoms of trait anxiety than the men. Mental strain in marriage/cohabitation and a low level of social integration were significant risk factors only among women. Compared with the reference group, both men and women with UCP perceived more stress at work, symptoms of depression and trait anxiety and had less social interaction. Gender differences in physical activity during leisure time were reported, as more UCP males than females were physically active, although the UCP patients, both genders, were significantly more sedentary compared with the reference group. The UCP patients, both sexes, had a higher BMI and reported a lower alcohol consumption/week than the reference group. After increasing until about 2000, the number of hospitalisations with a discharge diagnosis of UCP appears to have stabilised, while hospitalisations for angina and AMI have continuously declined. Compared with patients with angina and AMI, the overall one-year observed mortality rate in UCP patients was lower. Between 1997 and 2003 the one-year mortality among men with UCP was elevated by about one third, whereas women with UCP had no significant increase.

In conclusion, UCP was related to symptoms that influenced life in several ways. In general the gender differences were few and the mortality within one year was low. The thesis illustrates the importance of a deeper understanding of symptom perception to achieve an individualised care of patients with UCP.

Key words: Chest pain, unexplained chest pain, gender, daily life, psychosocial factors, stress, health-related quality of life.

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ORIGINAL PAPERS

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European Journal of Cardiovascular Nursing, 4:337-344.

- Π Janson Fagring A, Gaston-Johansson F, Kjellgren KI, Welin C (2007). Unexplained chest pain in relation to psychosocial factors and healthrelated quality of life in men and women. European Journal of Cardiovascular Nursing, 6:329-336.
- Janson Fagring A, Kjellgren KI, Rosengren A, Lissner L, Manhem III K, Welin C (2008). Depression, anxiety, stress, social interaction and health-related quality of life in men and women with unexplained chest pain.

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PAPER I - IV	

ABBREVIATIONS

AMI	Acute Myocardial Infarction
ACS	Acute Coronary Syndrome
BMI	Body Mass Index
CAD	Coronary Artery Disease
CHD	Coronary Heart Disease
ED	Emergency Department
HRQOL	Health-Related Quality of Life
INTERGENE	INTERplay between GENEtic susceptibility, environmental factors
IHD	Ischemic Heart Disease
ISSI scale	Interview Schedule of Social Interaction scale
MI	Myocardial Infarction
Non-CAD	Non-Coronary Artery Disease
NCCP	Non-Cardiac Chest Pain
POM	Pain-O-Meter
QOL	Quality Of Life
UCP	Unexplained Chest Pain

INTRODUCTION

Patients with chest pain, referred to hospital with suspected acute coronary syndrome (ACS), account for a large number of all the patients admitted to emergency departments (ED) (Goodacre et al., 2005). Murphy et al. (2004) found increasing hospital discharge rates for patients with chest pain (110%) and angina pectoris (79%), while the discharge rates for patients with myocardial infarction (MI) (33%) have declined from 1990 to 2000.

In Sweden, from 1998 to 2006, the number of patients hospitalised for unexplained chest pain (UCP), aged 16 to 69, rose from 9 280 to 11 427 men and 6 939 to 9 901 women (Figure 1) (The National Board of Health and Welfare, 2008). In addition, a large number of patients with UCP seeking care from primary health care have not been diagnosed and registered as UCP in the databases of the Swedish National Board of Health and Welfare. In primary health care, the number of patients with UCP almost doubled between 2001 and 2006 (The National Board of Health and Welfare, 2008). The increasing number of patients with UCP or by some researchers called non-cardiac chest pain is generating substantial health-care costs for society (Eslick et al., 2002; Eslick et al., 2003; Murphy et al., 2004).



Previous studies have found that those patients whose chest pain remains unexplained have symptoms that disable them for a long time. They often have a tendency to return repeatedly to the health service and do not appear to be satisfied with the medical care they receive (Aikens et al., 1999; Bass & Mayou, 2002; Robertson, 2006). Former studies of patients with UCP have shown that these patients appear to be younger,

have higher rates of anxiety and panic disorders and seek care more frequently compared with patients with IHD (Tew et al., 1995; Dammen et al., 2004; Eslick & Talley, 2004). Previous studies have indicated that patients with UCP often suffer from impaired quality of life and that UCP negatively impacts daily life (Aikens et al., 1999; Goodacre et al., 2001; Wong et al., 2002; Eslick et al., 2003; Jerlock et al., 2005). Studies have further indicated the importance of considering psychosocial factors, i.e. depression, anxiety and gender differences, when assessing patients with cardiac and non-cardiac diagnoses (Mayou & Thompson, 2002; Arslanian-Engoren, 2004; Granot et al., 2004; Chen et al., 2005; Mayou, 2005; Eken et al., 2008). Rosengren (2008) also draws attention to the fact that, in the care of the UCP patients, psychological aspects have to be considered.

This thesis is part of a larger project which previously investigated connections between UCP and psychosocial factors, such as coping strategies in general and relationships between coping and negative life events and sleep problems (Jerlock, 2007).

BACKGROUND

Pain

According to Turk and Melzack (2001), pain is the most common symptom that motivates people to seek health care. Pain can be defined in many different ways. More than 2 000 years ago, the ancient Greek society created an early biomedical model for health, illness and pain, based on the thoughts of Hippocrates and Galen, showing that pain occurred "when one of blood, phlegm, yellow bile, or black bile was either deficient or present in excess within the body" (Asmundson et al., 2004, p. 20). In the mid-seventeenth century, Descartes designed a model of pain as only a neurological formation (Asmundson et al., 2004). Melzack (1999) states that pain is a multidimensional experience caused by multiple influences and not only a relationship between pain and injury. Wall et al. (2006) define pain as "a personal, subjective experience that comprises sensory-discriminative, motivational-affective and cognitive-evaluative dimensions" (p. 291). The International Association for the Study of Pain (IASP) stresses that pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" and says that "pain is always subjective" (Merskey et al., 1994, p. 210).

Describing pain is a difficult matter as the professional and the patient may have different languages and different experiences when describing the pain. However, as pain is always a subjective experience, the patient's self-reported pain is possibly the most valid measurement (Wall et al., 2006). Pain can be divided into acute and chronic pain. Turk and Melzack (2001) describe acute pain as having a fairly brief duration (i.e. hours, days, or weeks) associated with tissue damage, inflammation or any process of disease. Chronic pain is described as a persisting pain (i.e. months or years), followed by a disease process, but this is not always correct, as it does not include pain that can be associated with acute recurrent pain (i.e. migraine headaches).

Classifying pain on the basis of diagnosis is another alternative, when evaluating methods, controlling and studying pain mechanisms and drawing distinctions between the concepts of nociception, pain and suffering. Professionals usually find that pain is something associated with pathology and nociceptive stimulation. Suffering, however, includes other factors such as interpersonal disturbances and psychosocial factors associated with the way pain can have an impact on the response to and perception of pain (Turk & Melzack, 2001). It is therefore essential to understand pain from both a biological and a psychological perspective in order to obtain a broader understanding of pain experience (Bullington et al., 2003; Asmundson et al., 2004).

Unexplained chest pain (UCP)

In the literature, there have been quite a few definitions of non-cardiac chest pain. Eslick and Talley (2004) state that non-cardiac chest pain is a "pain that had not been diagnosed as acute myocardial infarction (MI) or ischemic heart disease by a doctor" (p. 911). According to Fox and Forgacs (2006), "non-cardiac chest pain is considered to be central chest pain that resembles angina yet, after appropriate investigation,

its causes appears unrelated to the heart" (p. 445) and they state that it might be confusing. They therefore introduced the concept of unexplained chest pain (UCP). "Unexplained chest pain" may be preferable to the more frequently used "non-cardiac chest pain", because we still lack knowledge of whether it is an unrecognised cardiac disease. In this thesis, UCP was defined as a chest pain free from any history of heart disease or other known organic cause explaining the chest pain, e.g. musculoskeletal and gastro-esophageal disorders.

Incidence and mortality among patients with acute coronary syndromes

MacIntyre at al. (2006) have studied the hospitalisation trends for suspected acute coronary syndromes (ACS). They found that the number of patients hospitalised with chest pain was increasing steadily every year and that the hospitalisation rates for women with chest pain, aged 55 years and younger, were increasing more than those for men. Among patients diagnosed with AMI, on the other hand, the hospitalisation rates had declined by about 30%. Even though women referred to EDs for coronary symptoms were not admitted to cardiac wards as frequently as men, or did not receive coronary revascularisation procedures to the same extent, the outcome regarding one-year mortality were no worse (Kaul et al., 2007).

Gender differences in the perception of chest pain in relation to diagnosed unstable angina pectoris and MI have been reported, demonstrating that women perceived higher levels of pain intensity and had more symptoms compared with men (Miller, 2002; Granot et al., 2004; Chen et al., 2005). However, Perers et al. (2005) found no significant differences in treatment and outcome between men and women suffering acute coronary syndromes. Nor did women suffer more severe complications or have significantly higher 30-day mortality than men.

Illness and disease, symptoms and signs

In the care of UCP patients, the understanding of illness and disease and symptoms and signs might require some reflection. Eisenberg (1977) draws a distinction between disease and illness, stating that the physician diagnoses and treats diseases but the patients suffer from illness. Illness is a perception and disease is abnormalities in the function of the bodily organs and systems, as explained in the scientific paradigm of modern medicine. There might also be a discrepancy between the disease diagnosed by the physician and the patient's perception of illness. Kleinman (1988) stresses that there is a total distinction between illness and disease. Illness is *"how the sick person, and the members of the family or wider social network perceive, live with, and respond to symptoms and disability, the illness experience includes, categorizing, and explaining the forms of distress caused by those pathophysiological processes"* (p. 4, 5).

If disease is a problem only from the practitioner's perspective and is not seen in a wider perspective, the consequences can be a failure as exemplified by Kleinman: "when chest pain is reduced to chronic coronary artery disease, while the patient's fear, the family's frustration, the job conflict, the sexual impotence, and the financial

crises go undiagnosed and unaddressed, it is a failure" (p. 6). According to Foucault (1994), a disease, in the medical tradition of the eighteenth century, was looked upon in terms of symptoms and signs, distinguished from each other by both the semantic value and the morphology. The symptom "is the form in which the disease is presented". The sign "announces: the prognostic sign, what will happen; the anamnestic sign, what has happened, the diagnostic sign, what is now taking place" (p. 90). According to Foucault, symptoms and signs are almost the same thing; the only difference is that "every symptom is a sign but not every sign is a symptom" (p. 93). Dodd et al. (2001) stated that both symptoms and signs might be important when patients seek health care, as the symptom is the individual's subjective perception and the sign might also be observed by others. As a result, the absence of symptoms and signs does not necessarily indicate perceived well-being and health.

It has been well documented that there are cultural differences in the way symptoms of illness, e.g. pain, are expressed (Eisenberg & Kleinman, 1981; Kirmayer et al., 2004). In view of this, it is essential to confirm these patients' suffering and help them to understand that emotions and stress can also influence their physical health (Kirmayer et al., 2004). Kirmayer and Young (1998) stated that somatisation can be interpreted as non-specific indicators of psychiatric illness, as many patients with panic disorder or mixtures of depression-anxiety, for example, also present somatic symptoms. Somatisation could also be a question of educational level.

Several authors have pointed out how important it could be to listen to illness narratives, as this lends consistency to the patients' suffering and perceived symptoms. Few patients spontaneously talk about their concerns; instead they sometimes create explanation models, which can include serious medical conditions. The professionals must therefore actively and carefully listen in order to recognise the patients' own ideas about their symptoms, verbally transmitted through "clues" (Lang et al., 2000). Focusing on professional nursing care, Skott (2001) said that an essential part of the knowledge of sickness is obtained through communication and verbally narrated stories. The story the patient tells often includes more than it appears to do and the nurse should assume the interpreting role between the world of medicine and the patient's story regarding the perception of sickness.

Benner and Wrubel (1989) emphasise the importance of understanding the relationships and differences between health, illness and disease, inspiring the nurse to listen to the patient's illness stories. The treatment and cure of illness might be easier if the patient could be given some help to find a meaning in the illness, even when no cure is possible. Understanding the meaning could be likened to healing, avoiding feelings of alienation and the loss of social interactions perceived with illness, for example.

Gender and pain

Gender identity is "an individual's self-conception as being male or female, as distinguished from actual biological sex. Gender identity is not fixed at birth; both physiologic and social factors contribute to the early establishment of a core identity, which is modified and expanded by social factors as the child matures" (Encyclopedia Britannica, 2008). In the western industrialised countries, there is a saying "women get sick and men die", meaning that women have a longer life expectancy in terms of mortality but they also have higher rates of acute and chronic diseases (Bendelow, 2000). Women use more medical services and have higher rates of prescriptions compared with men. Gender differences are also seen in mental health, as women have higher rates of psychiatric admissions to the heath service.

According to Bendelow, gender differences in morbidity and mortality are biological aspects of illness risks, risks of illness acquired from gender roles, different health and illness reporting behaviours and differential diagnoses and treatments. In the epidemiological pattern of pain, women's pain is not always regarded as being as serious as men's. Fillingim (2000) stated that the female and male organisms differ in their response to pain. This is a fairly complex issue and there still is a lack of knowledge and understanding. As a result, different studies have presented various explanations of the gender differences, such as psychosocial explanations; *"sex role expectancies (i.e. feminity vs. masculinity), cognitive/affective factors (e.g. anxiety, coping, and self-efficacy) and social learning"* (Fillingim, 2000, p. 4), concluding that gender-related factors are only some of many variables. Other factors such as age, disease and psychosocial status might be even more important.

Gender differences in perceived chest pain and diagnosis have been found in several previous studies. Male patients more frequently than females were diagnosed with cardiac chest pain instead of non-cardiac chest pain (Keogh et al., 2004; Omran & Al-Hassan, 2006). Women with coronary heart disease symptoms presented more undifferentiated symptoms than men and women also had difficulty interpreting their symptoms, ending in delayed admission to EDs (Lockyer, 2005; Omran & Al-Hassan, 2006). When comparing men and women with cardiac diseases, Nau et al. (2005) found that women rated their symptoms as being less severe than men. Previous studies have also indicated that women perceiving pain and unexplained disorders often feel that their symptoms have been ignored by the physician and that they had difficulty being listened to seriously (Malterud, 1998; Werner & Malterud, 2003; Werner et al., 2004). White and Johnson (2000) reported that men with chest pain, because of their self-conception of being healthy, sometimes deny and explain the pain away.

Psychosocial factors in relation to pain perception

Previous studies have indicated that men and women use different ways of mastering pain. Men generally use problem-focused coping, while women use more emotionally focused coping such as social interaction or lay the blame upon themselves (Fillingim, 2000; Jerlock & Gaston-Johansson et al., 2006).

Fillingim (2000) stated that catastrophising might be an important factor to consider in the assessment and treatment of pain, associated with increased negative pain perception, worries about the future, lack of control and finding life overwhelming. In the same way, Asmundson et al. (2004) found relationships between negative affectivity, catastrophising, anxiety sensitivity and the fear of pain associated with emotional disorders such as panic disorder, depression and post-traumatic stress disorder.

Depression, anxiety and panic disorder

The prevalence of major depressive disorders is twice as high in women as in men, depending on hormones and different sex-related psychosocial stressors, for example (Sadock et al., 2007). Sadock et al. define depression as a "mental state characterized by feelings of sadness, loneliness, despair, low self-esteem, and self-reproach; accompanying signs include psychomotor retardation or, at times, agitation, withdrawal from interpersonal contact, and vegetative symptoms, such as insomnia and anorexia" (p. 276).

In the general population, anxiety disorders are the most common mental disorders, twice as frequent in females as in males, chronic and followed by significant morbidity. Sadock et al. (2007) define anxiety as "*a feeling of apprehension caused by anticipation of danger, which may be internal or external*" (p. 274).

Panic disorder has been described in the literature in relation to patients with UCP. Sadock et al. (2007) define panic disorder as "a discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes: palpitations, pounding heart, or accelerated heart rate, sweating, trembling or shaking, sensations of shortness of breath or smothering" (p. 590).

Diagnosing panic disorder can sometimes be a complicated matter. Several previous studies have found that chest pain patients suffering from panic disorders related to psychological distress are quite frequently referred to cardiology departments and do not receive adequate treatment for their panic (Dammen et al., 1999; Bringager et al., 2004; Dammen et al., 2004). Hamer and McCallin (2006) reported similar problems in the nursing assessment when differentiating cardiac pain from panic disorders at EDs.

Social interaction/social support

According to Cobb (1976), social support begins in the mother's uterus and continues throughout life from different individuals in society, but, in the end, the focus of support often lies with family members. Social support means that the individual is a member of the network and is worth loving and being cared for. Hupcey (1998) stated that the concept of social support is a multi-faceted concept and there is no agreement among researchers about how to understand and define it. In the mid-1970s to 1980, social support was an interaction and was fairly concrete.

More recently, social support has become more abstract and confusing and almost all interactions can be defined as social support. Both positive and negative influences have to be regarded as part of social support. Social support can be understood as "a dynamic process that includes the interaction between the provider and recipient, and varies by recipient and provider" (Hupcey, 1998, p. 1235). Orth-Gomer et al. (1998) have found that social isolation, a low level of social support and small social networks are associated with unwholesome health behaviours, increased morbidity and mortality.

Earlier studies of social networks and pain inference revealed positive associations between social networks and having continuous contact with a large number of children, especially in men (Peat et al., 2004), although male patients when suffering from pain tended to have little energy for social life (Paulson et al., 2002). In women with suspected coronary diseases, the findings indicated an association between social networks and lower mortality rates (Rutledge et al., 2004), while individuals with a lack of social support ran an increased risk of CHD (Lett et al., 2005).

Stress at work and mental strain in marriage or cohabitation

Lazarus and Folkman (1984) define stress as "the relationship between the person and the environment, which takes into account characteristics of the person on the one hand, and the nature of the environmental event on the other" (p. 21). Previous studies have demonstrated that stress at work has various health effects and is "associated with specific factors in the environment having different strain consequences. Stress is an unpleasant emotional experience associated with feelings of tension, irritation, annoyance, dread, anxiety" (Manning el al., 1996, p. 100).

Scnall et al. (1990) concluded that job strain arises when the individual has little decision latitude at work and high psychological demands. Further, Kristensen (1996) stated that job strain can be related to psychological strain, including a number of different conditions such as cardiovascular diseases, sleeping problems, anxiety and depression. Relationships between self-reported symptoms such stress, depression or heart symptoms, must not, however, be understood as relationships between health and work. These relationships instead indicate the probability of symptoms reported at individual level and could therefore be a measurement problem. Work stressors must therefore be measured in different ways, such as non-dependent and self-measured. Previous research has, for example, demonstrated gender differences in perceiving stress and, according to Lundberg (1996), studies analysing the role played by sex hormones in stress responses are insufficient. Psychological factors and the patterns of gender roles might have more influence on the physiological response to stress. Blom (2005) found, when studying psychosocial risk factors in women with coronary heart disease, that social support had an important impact on marital stress.

Quality of life and health-related quality of life

The World Health Organisation Quality of Life group has defined quality of life (QOL) as "*individuals*' *perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, stan-dards and concerns*" (WHO, 1998, p. 551). The domains included are physical health, psychological, social relationships and environment and the definition concludes that QOL is always a subjective evaluation.

Measuring health-related quality of life (HRQOL) has become a common and essential part of clinical research. It is, however, important to make clear definitions of HRQOL in order to transform the concept from a philosophical and phenomenological concept into a concrete measurement (Shumaker & Berzon, 1995). There is agreement among researchers that HRQOL is a multi-dimensional concept, although no consensus has yet been reached about the "key" dimensions. Schumacher and Berzon suggest the following definition: "Health-related quality of life refers to people's subjective evaluations of the influences of their current health status, health care, and health promoting activities on their ability to achieve and maintain a level of overall functioning that allows them to purse valued life goals and that is reflected in their general well-being" (Shumaker & Berzon, 1995, p. 7).

Several previous studies have indicated that psychological problems and impaired quality of life are common among chest pain patients (Goodacre et al., 2001; Wong et al., 2002; Biggs et al., 2004; Eslick & Talley, 2004; Jerlock et al., 2008). When comparing HRQOL in CAD patients and patients without CAD, HRQOL was significantly lower among CAD patients (Unsar et al., 2007).

AIMS

The overall aim of this thesis was to describe and analyse symptom perception, psychosocial factors, health-related quality of life (HRQOL) and outcome of unexplained chest pain (UCP) in men and women.

Specific aims

- To describe the experience of unexplained chest pain and its influence on daily life situation in men and women (Paper I)
- To analyse gender differences regarding pain characteristics, psychosocial factors and health-related quality of life among patients diagnosed unexplained chest pain (Paper II)
- To analyse differences between men and women with UCP and a reference group in terms of psychosocial factors as depression, anxiety, stress, social interaction and health-related quality of life (HRQOL) (Paper III)
- To study trends in incidence and prognosis in patients hospitalised with UCP, angina and AMI in Sweden between 1987 and 2003 (Paper IV)

METHODS

Both qualitative and quantitative methods have been used in this thesis. The UCP patients' symptoms and their influence on daily life in a gender perspective were explored in Paper I using open interview questions. A cross-sectional design was used in Paper II, assessing pain characteristics using the Pain-O-Meter and measuring psychosocial factors and HRQOL using a self-administered questionnaire. In Paper III, psychosocial factors and HRQOL were compared between UCP patients admitted consecutively to an ED or as in-patients on a medical ward and a reference group, i.e. a subsample from the INTERGENE population study. Paper IV was a register study, investigating trends in incidence and outcome among patients first hospitalised with UCP, angina pectoris and AMI in Sweden. All the data in Papers II and III were collected by the two investigators in the project (AJF and M Jerlock). Table 1 shows an overview of the included Papers and Figure 2 the study populations.

Study populations and investigation procedures

Paper I

The participants, 11 men and 9 women (age range 31-62), were in-patients on a medical ward at Sahlgrenska University Hospital/Östra in Gothenburg, Sweden, for chest pain observation and they were discharged with the diagnosis of UCP. The data were collected between October 2003 and March 2004. The inclusion criteria were men and women aged 16-69 years, Swedish speaking and recently experiencing recurrent chest pain. All the included patients were first admitted to the ED for chest pain and, after an examination by a physician, they were admitted to stay overnight on a medical ward for further observation. The nurse in charge of the medical ward made the first decision about the patient's inclusion in the study, based on the diagnosis of UCP and the patient's condition. Subsequently, after verbal and written informed consent was obtained from the patient, the interview was carried out (AJF) in different places in accordance with the patients' wishes. In the interviews, the interviewee talked about his/her chest pain using the following two open interview questions: 1) Can you tell me about your chest pain? 2) Can you tell me about your daily life situation? All the interviews were audio recorded with the patients' permission and lasted between 30 to 60 minutes and were transcribed verbatim (AJF).

Papers II and III

The data were collected at the ED at Sahlgrenska University Hospital/Östra in Gothenburg, Sweden, between December 2002 and September 2003. The patients were included during office hours and not during holidays or weekends as the data collection was only performed by the two investigators (AJF and MJ). Considered for inclusion were patients consecutively admitted to the ED for acute chest pain, judged by a physician to have no organic cause of their chest pain and free from any history of heart disease. The patients had to be Swedish speaking in order to be able to complete the questionnaire. The recruited patients were first assessed by the staff according to the standard ED routines. Patients fulfilling the inclusion criteria were subsequently asked to participate in the study, after verbal and written informed consent was ob-

	Methods	Inclusion criteria	Exclusion criteria	Subjects	Measurements	Data analyses
Paper I Description of unexplained chest pain and its influence on daily life in men and women	Interview	16-69 years old Diagnosed as UCP >1 event of chest pain	Language difficulties Previously diagnosed IHD	20 UCP patients: 11 men, 9 women	Open-ended interviews	Content analysis
Paper II Unexplained chest pain in relation to psychosocial factors and health-related quality of life in men and women	Cross- sectional	16-69 years old Diagnosed as UCP	Poor general condition Language difficulties Previously diagnosed IHD	179 UCP patients: 101 men, 78 women	Pain-O-Meter Zung self-rating depression scale Trait-anxiety inventory scale Interview schedule for social interaction (ISSI) SF36	Student's two-tailed t-test Chi-square test Spearman's correlation test Cronbach's alpha
Paper III Depression, anxiety, stress, social interaction and health- related quality of life in men and women with unexplained	Case control study	25-69 years old Diagnosed as UCP	Poor general condition Language difficulties < 25 years old Known IHD	231 UCP patients: 127 men, 104 women	Zung self-raiting depression scale Trait-anxiety inventory scale Interview scheudule for social interaction (ISSI) SF36	Student's two-tailed t-test Chi-square test Odds ratio Multivariate logistic stepwise regression
chest pain		25-69 years old Participation in the InterGene population-based study	Known IHD	1069 reference participants: 490 men, 579 women		models
Paper IV Trends in incidence and mortality among patients hospitalised with unexplained chest pain compared with angina pectoris and acute myocardial infarction	Prospective register study	25-84 years old First hospitalisation with UCP, angina and AMI		168 967 UCP patients 192 842 Angina patients 198 070 AMI patients		Survival analysis

Table 1. Overview of included papers

tained. The patients were then asked to assess the worst pain during the last 24 hours and to describe their perceived chest pain using a pain assessment tool (Gaston-Johansson, 1996). The patients also marked on a drawing of a human figure in the questionnaire all locations of perceived pain, during the last four weeks (Paper II). Finally, the patients (Papers II and III) completed a self-administered questionnaire consisting of questions about demographic, biomedical and psychosocial factors and HRQOL. The ED patients filled in the questionnaire shortly after arriving at the hospital and the in-patients did so within 24 hours after arrival.

In Paper II 179 patients (101 men and 78 women, mean age 45.3 years) aged 16 to 69 participated in the study, with a participation rate of 73.4%. In Paper III the UCP patients were 25 to 69 years in order to match to the participants in the reference group. In all, 231 patients (127 men and 104 women) took part in this study (78%). Of these, 157 were investigated in the ED and 74 were in-patients investigated after being admitted to the medical ward for further observation.

The reference group in Paper III consisted of residents of Gothenburg aged 25-69 years and free of clinical heart disease and they were recruited from the INTERGENE study. INTERGENE is a population-based study assessing the interplay between genetic susceptibility, environmental factors, lifestyle and psychosocial background as risk factors for chronic diseases and cardiovascular disease (the study procedure is described in detail at http://www2.sahlgrenska.gu.se/intergene/eng/project.jsp). The referents were assessed according to the protocol for the INTERGENE study (Berg et al., 2005). Of the recruited sample (n=2 422), 1 477 (61%) came to the screening during the study period. As the psychosocial questionnaires including self-reported HRQOL were not presented to the participants in the primary survey but in a secondary one, 380 people (189 men and 191 women) did not complete the questionnaires as they did not participate in the secondary survey. In all, 1 069 individuals (490 men and 579 women) participated (72% of those screened and free from any history of heart disease).

Paper IV

The data were collected from the Swedish National Hospital Discharge Register. All first hospitalisations, from 1987 to 2003, with a diagnosis of UCP, angina pectoris and AMI and aged 25 to 84, were recorded. The data comprise 19 of the 24 Swedish counties, which is 85% of the Swedish population in this age group. The International Classification of Diseases (ICD) version 9 (ICD 9) was used from 1987, while version 10 (ICD 10) was used from 1997 and onwards. UCP was defined as 786F (ICD 9); and R07.2, R07.3 and R07.4 (ICD 10). The diagnostic codes for angina were 411B and 413 (ICD 9) and I20 (ICD 10), while they were 410 (ICD 9) and I21 (ICD 10) for AMI. In all (n=559 879), 168 967 patients with UCP, 192 842 patients with angina pectoris and 198 070 patients with AMI were registered and they were followed for one year with respect to mortality.



Figure 2. Study populations.

Measurements (Papers II and III)

Demographics and background characteristics assessed in the questionnaire were recorded from both the UCP patients and the reference group and the items included are shown in Table 2.

Demographics and			Amelyand			
background Response alternatives Page		Paper	variables		Paper	
characteristics			Vallables			
Age	Years		Mean		111	
Marital status	*Single (1)		Single status (0-1)	Ш	Ш	
	*Married/cohabitating (0)					
	*Divorced (1)					
	*Widow/er (1)					
Education	*Compulsory (0)		University education (0-1)	Ш	III	
	*Secondary school (0)					
	*University (1)					
	*Other education (0)					
Work status	*Full time (1)		Employed (0-1)	Ш	111	
	*Part time (1)					
	*Retired (0)					
	*Early retirement/disability pension, full time (0)					
	*Early retirement/disability pension, part time					
	(0)					
	*Unemployed (0)					
Country of birth	*Sweden (1)		*Sweden	II		
	^Finland (2)		*Nordic countries outside			
	*Nordic countries outside Sweden (2)		Sweden			
	*Eurpean country outside Nordic countries (3)		"Outside Nordic countries			
	Country outside Europe (3)					
Immigrant	Yes/no		Immigrant (0-1)			
Physical activity in	*Sedentary (1)	11	Sedentary (0-1)		ш	
leisure time	[^] Moderate exercise (i.e. walking, riding bicycle,					
	Ight gardening for a minimum of 4 hours) (0)					
	Regular exercise and training (i.e.strendos					
	*Intense training or competitive sport (0)					
	intense training of competitive sport (0)					
Current smokers	Yes/no		Current smokers (0-1)	II	III	
Alcohol consumption	Frequency and amount of beer, wine and		Alcohol g/week		III	
Mainht and bainht	spirits		Dedu Mass Index (DMI)			
Neight and height	kg, cm		Body Mass Index (BMI)			
Diabetes, physician	Yes/no		Diabetes (0-1)	11	111	
Hypertension.	Yes/no		Hypertension (0-1)	11		
physician confirmed			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
Chest pain, walking	Yes/no		Walking uphill (0-1)			
uphill						
Chest pain, walking	Yes/no		Walking on flat ground (0-1)	Ш		
on flat ground						
Admitted for chest	Yes/no		Admitted in the last 3	II		
pain in the last 3			months (0-1)			
Days on sick leave in	Number of days		Mean	Ш		
the last year						
Use of drugs in the	[•] Daily (1)		Once a week or more (0-1)	11		
last month ^a	"Every week (1)					
	Less inan once a week (U)					
	not at all in the last month (U)					

Table 2. Demographics and background characteristics assessed in the questionnaire

^a Analgesics, sleeping pills, sedatives

The measurements used to describe and analyse symptom perceptions, psychosocial factors and HRQOL are described below.

Pain-O-Meter (Paper II)

The patients' chest pain was measured using the Pain-O-Meter (POM), a self-assessment pain tool developed for the purposes of improving the assessment and management of pain in patients with acute and chronic pain (Gaston-Johansson, 1996). Using the POM, chest pain intensity, quality, location and duration can be assessed. To assess pain intensity, the POM-VAS (r=.88, p<001) was used and pain quality was assessed by the POM-Words (WDS) (r=.84, p<001). The POM-VAS is an analogue scale with scores of 0 to 10 and the POM-WDS is a list of 12 sensory (e.g. "pressing" and "burning") and 11 affective (e.g. "worrying" and "frightening") word descriptors. The sensory and affective words on the POM represent general words for pain expression with intensity values determined in research (Gaston-Johansson, 1996). Assessing pain intensity is the quantitative way of estimating the magnitude and severity of perceived pain and the pain quality is the emotional experience associated with the pain (Turk & Melzack, 2001).

Interview schedule for social interaction (ISSI)

Social interactions were measured by the ISSI scale consisting of four subscales; the availability of attachment (AVAT), the perceived adequacy of attachment (ADAT), the availability of social integration (AVSI) and the adequacy of social integration (ADSI) (Henderson et al., 1980; Undén AL, 1989; Welin, 1995). Only the two sub-scales, the AVSI and AVAT, were used in this thesis. The AVSI scale, assessing the availability of social integration, consists of six questions, such as "These days, how many people with similar interests to you do you have contact with?" The response alternatives (recoded score values) are: "none" (0), "1-2 people" (1), "3-5" (2), "6-10" (3), "11-15" (4) and "more than 15" (5). The scale score range is 0-30, where high scores indicate a high level of social integration. The AVAT scale assesses the availability of attachment and consists of eight questions, such as "Is there any particular person you feel you can lean on?" The response alternatives (re-coded score values) are: "no" (0), either "yes, but do not need it", or "are not sure", or "not enough" (1), "yes" (2). Scale scores range between 0 and 16, where high scores indicate high attachment (Table 3).

Zung self-rating depression scale

Symptoms of depression were assessed by the Zung Self-Rating Depression scale (Zung, 1965, 1967; Welin, 1995). The scale assesses physiological and psychological symptoms and can also be used in non-psychiatric settings as a diagnostic tool identifying symptoms of depression in patients with chronic pain, for example. The scale is made up of 20 items, such as "I feel down-hearted and blue" or "I feel hopeful about the future". The response alternatives are "a little of the time" (1), "some of the time" (2), "good part of the time" (3) and "most of the time" (4). Higher scores indicate more symptoms of depression and the scores range between 20 and 80. In the Zung Self-Rating Depression Scale, mild depression is equal to 50-59 scores, moderate depression to 60-69 scores and severe depression to \geq 70 (Zung, 1967). Symptoms of

depression among the UCP patients were calculated as a score of \geq 39, which represented the highest quintile in a normative population (Welin, 1995) (Table 3).

Trait-anxiety inventory scale

The UCP patients' and the referents' symptoms of trait anxiety was assessed by the Trait-Anxiety Inventory scale, a self-reported questionnaire consisting of 20 items measuring general feelings, such as "I worry too much over something that really doesn't matter". The ratings are made on a four-point scale: "almost never" (1), "sometimes" (2), "often" (3) and "almost always" (4). Scale scores range between 20 and 80, where high scores indicate high degrees of symptoms of trait anxiety (Spielberg CD, 1968; Welin, 1995) (Table 3).

Health-related quality of life (HRQOL)

The SF 36 was used to measure the HRQOL consisting of eight scales assessing both physical and mental domains according to self-reported HRQOL. The scales measuring physical health are *physical functioning* (PF), e.g. vigorous and moderate activities, *role-physical* (RP), i.e. limitations in performing work or other activities, *bodily pain* (BP), i.e. bodily pain during the past four weeks, and *general health* (GH), with the response alternatives: "excellent", "very good", "good", "fair" and "poor". The scales measuring mental health are *vitality* (VT), i.e. energy or tiredness, *social functioning* (SF), i.e. the extent to which physical health or emotional problems have interfered with social activities during the last four weeks, *role emotional* (RE), i.e. accomplished less than you like, and *mental health* (MH), i.e. nervous or happy person. Higher scores indicate better health-related quality of life and scores range between 0 and 100 (Cronbach's alpha range between .79 and .93) (Sullivan, 1992; Sullivan & Karlsson, 1994). In Paper II, only four of the assessed scales were analysed: *physical functioning* (PF), *general health* (GH), *vitality* (VT) and *mental health* (MH). In Paper III, all eight scales were analysed (Table 3).

Assessment	Scale	Items	Scale score	Reliability	References
Social integration Social attachment	Interview Schedule for Social Interaction	6 8	0-30 0-16	Test-retest reliability 0.75 Test-retest reliability 0.76	Henderson et al. 1980 Undén et al. 1989
Symptoms of depression	Zung Self-Rating Depression Scale	20	20-80	Chronbach's alpha 0.92	Zung 1965
Trait-anxiety	Trait-Anxiety Inventory	20	20-80	Chronbach's alpha 0.83 to 0.92	Spielberg 1968
Health-related quality of life	SF 36	36	0-100	Chronbach's alpha 0.79 to 0.93	Sullivan & Karlsson 1994

 Table 3. Scales used and their reliability

Stress at work and stress at home

In Paper II, perceived stress at work and stress at home were assessed with two items and, in Paper III, only perceived stress at work was assessed (response alternatives; never perceived stress (0), some period of stress (1), some period of stress during the last five years (2), several periods of stress during the last five years (3), permanent stress during the last year (4) and permanent stress during the last five years (5) (Rosengren et al., 2004).

Mental strain in the marriage or cohabitation

The way the participants perceived their marriage or cohabitation was assessed with two items: 1; "How do you think your marriage or cohabitation is?", with response alternatives: "very happy" (1), "fairly happy" (2), "difficult to say" (3), "fairly unhappy" (4) and "very unhappy" (5), and 2; "How often do you have difficulty getting along with your wife or husband or cohabitant?", with response alternatives; "never" (1), "seldom" (2), "sometimes" (3), "often" (4) and "almost all the time" (5) (Welin, 1995).

Analyses

Content analysis (Paper I)

The data in Paper I were analysed by content analysis. Krippendorff (2004) defines content analysis as "a research technique for making replicable and valid inferences from texts (or other meaningful matter) to the contexts of their use" (p. 18). Content analysis is a reliable technique which is expected to follow specific procedures (searching for codes, sub-categories and categories/themes from meaning units in the texts) at the analysis stage. It is also a scientific tool providing knowledge, new insights and replicable findings. To make the findings replicable, every content analysis requires an explicated context in which the texts are investigated. According to Krippendorff (2004), a "context is always constructed by someone, here the content analyses, no matter how hard they may try to objectify it" (p. 25).

There are two different ways of using content analysis, the quantitative approach and the qualitative approach in accordance with Graneheim & Lundman (2004). The characteristics of qualitative content analyses are manifest and latent content. Manifest content is what the text just says, usually presented in categories, while latent content is what the text talks about, often presented in themes.

The texts in Paper I were worked up in several steps; firstly, the texts were read and a written conclusion was then drawn from each interview. Subsequently, the whole text was re-read and divided into two parts embracing the patients' descriptions and the consequences of their chest pain and daily life situation. Important meaning units emerged when reading the texts very carefully and condensed meaning units were then selected. The analysis of the text continued by searching for codes, sub-categories and categories/themes, which were finally interpreted as descriptions and manifest content/categories. In the Paper, the descriptions and the consequences of chest pain are illustrated solely using the patients' descriptions, as this appeared to be the most valid way of probing the true core content of the narratives. From the narratives relating to the daily life situation, eight sub-categories emerged from the codes and they were then reduced and presented as four categories. The text was independently analysed during the whole procedure by one of the co-authors to ensure credibility.

Statistical methods (Papers II, III and IV)

The analyses in Papers II and III were carried out using the Statistical Analysis System (SAS) 8.2, (SAS Institute Inc., Cary, NC). In Paper II, differences between men and women regarding pain characteristics, demographics and psychosocial factors were analysed using the chi-square test for discrete variables and Student's t-test for continuous variables. Correlations between continuous and discrete variables were tested using Spearman's correlation coefficient. In Paper III, differences between the UCP patients and the reference group in terms of demographics and psychosocial factors were tested using the chi-square test for discrete variables and using Student's t-test for continuous variables. Odds ratios were calculated for selected background characteristics and psychosocial variables simultaneously controlling for age, smoking, hypertension and diabetes. Multivariate logistic stepwise regression models were also used. In step 1, all the variables were included if p<0.10 in the univariate analysis. In step 2, variables were included if p<0.10 in step 1. In Paper IV, totals, age and gender characteristics, observed and expected one-year mortality rate per 1000 were computed and presented for the three patient categories; UCP, angina and AMI. The expected one-year mortality rate was based on the age-, gender- and calendar-yearspecific death rates of the national population. Age-standardised annual incidence rates per 100 000 first hospitalisations for UCP, angina and AMI were also calculated using the direct method, with the 2004 population as the standard. In Paper IV, the analyses were carried out using the Statistical Analysis System (SAS), version 9.1, and the R statistical computing system, version 2.7.0. The statistical significance used in the studies assumed a p-value < 0.05.

Ethical approval and considerations

The studies were approved by the Ethics Committee at the University of Gothenburg, Sweden (study codes: Papers I-III 169-02 and Paper IV 148-07), and complied with the World Medical Association Helsinki Declaration (WMA, 2000). The interviews in Paper I were conducted after both verbal and written informed consent was received from each patient. The patients were also told that their participation was voluntary, confidentiality was guaranteed and if, at any time, they felt uncomfortable, they could withdraw without this having any negative impact on their care. It is vital to be aware of the difficulty involved in being a patient who declines to participate in a study, after being personally asked by the investigator. Several of the participants did not have Sweden as their place of birth and it was therefore essential to show respect for their sometimes different customs. The interviews were carried out in different places, in accordance with the participants' wishes and all the interviews were conducted by the same interviewer (AJF).

The procedure for the data collection for the quantitative studies (Papers II and III) was similar; after verbal and written informed consent was obtained from each pa-

tient, the patients were told that participation was voluntary and that confidentiality was guaranteed. The data were collected solely by the two investigators (AJF, MJ). Even though the questionnaires contained 184 items, most of the participants said that it was interesting to reflect over the questions and that the waiting time for the physicians' assessment at the ED might pass more quickly. Even so, all the research has to be balanced against possible harm caused to the participants and the scientific value. Moreover, corroborating Polit and Beck (2004), when using humans as participants in research, it is of the greatest importance to protect their rights.

Finally, Paper IV was a register study in which the recorded data were obtained from the Swedish National Hospital Discharge Register. As Sweden, together with Scotland, Finland and Denmark, has the unique opportunity to link personal identity numbers and registers together, this must be considered with the same confidentiality as all other research involving human beings.

RESULTS

The results of the original papers are presented separately and in chronological order. Readers are referred to the original papers.

Paper I

The results in Paper I contain the narratives of eleven men and nine women, describing their chest pain and its effect on their daily life. Most of the participants, both sexes, were married and, in addition to Sweden, various countries of birth were reported; Finland, Macedonian, Iran and Poland (Table 1, Paper I). The results of the interviews are presented in two parts containing descriptions and consequences of chest pain and daily life situation, focused on gender.

Descriptions and consequences of chest pain

Most of the participants had a pronounced need to talk about their chest pain and its consequences. They used different words when describing the chest pain such as "pressure" and cramp", perceived with more similarities than differences between the men and the women (Table 3 and 4, Paper I). Several of the participants used meta-phors to describe how they perceived the pain. Descriptions of physical, psychological and social consequences caused by the chest pain were given. They suffered from symptoms such as tachycardia and fatigue and both men and women talked about the fear of having a heart attack, the fear of death and dying. In the narratives, the participants admitted that they were worried, as they did not know what was causing their recurrent chest pain.

Daily life situation

The results of the narratives concerning the patients' daily life situation are presented in four categories and eight sub-categories, in a gender perspective. The daily life situation comprises *the person, the work, the home and the family* and *friends*, presented in four categories (Table 5, Paper I). From the four categories, eight sub-categories emerged containing *the person*: fast tempo in life, physical activity, tiredness, *the work*: fast work pace and stress, *the home and the family*: looking after the house, taking care of the children and relaxation. The fourth category was made up solely of *friends* without any sub-category. The men in particular stated that they experienced a fast tempo in life and perceived stress at work. Tiredness was described by both sexes. The women in particular said that their daily walks were a recurrent, popular activity. Both men and women described taking care of the children as an important part of life. Few of the participants had contact with other people apart from the family and this resulted in a weak social network, especially for the men.

Paper II

Gender differences relating to pain characteristics, psychosocial factors and HRQOL among patients with UCP were investigated in Paper II.

Demographics

The results revealed that one third of both UCP males and UCP females were born outside Sweden. More women than men had only completed compulsory education. A quarter of both men and women reported that they were sedentary during their leisure time and gender differences were found in physical activity during leisure time (p<0.01), as more men than women were active during their leisure time (25% versus 8%). The results did not reveal any significant differences between men and women regarding age, marital status, country of birth or work status (Table 1, Paper II).

Biomedical risk factors

The results showed significant gender differences regarding days of sick leave, smoking and BMI. The UCP women were on sick leave for 28 days versus 17 days for the UCP men (p<0.001), were current smokers to a greater extent (p<0.01), while the UCP men were more often overweight (p<0.001). The results did not reveal any significant gender differences regarding chest pain walking uphill or walking on flat ground, chest pain earlier in the last three months, known diabetes, hypertension or using drugs (analgesics, sleeping pills or sedatives) (Table 2, Paper II).

Pain intensity and pain quality

When rating the intensity of the worst chest pain during the last 24 hours (POM-VAS scale 0 to 10), the results did not reveal any significant difference between men (mean 6.1) and women (mean 6.5). The frequency of sensory and affective word descriptors from the POM revealed few significant differences in terms of gender, apart from "burning" and "frightening" being used more frequently by the women and "torturing" by the men. "Pressing" was the most frequently used sensory word descriptor and "worrying" the most frequently used affective word descriptor, according to both men and women (Table 3, Paper II).

Psychosocial factors

The psychosocial factors measured in Paper II were stress, mental strain in the marriage/cohabitation, symptoms of depression and trait anxiety and social interaction. The results revealed that almost half of UCP men and women perceived constant stress at work during the last year and that the women more often than the men had perceived constant stress at home. In the same way, women more often than men reported difficulty getting along in the marriage and cohabitation. Regarding symptoms of depression and trait anxiety, significant gender differences were found, where the women reported depressive symptoms (p<0.01) and symptoms of trait anxiety (p=0.01) to a greater extent than the men (Table 4, Paper II). The results also showed that there was a significant association between current smoking and pain intensity (p<0.01) among UCP men, while the UCP women reported less pain intensity with increasing age (p<0.05).

Health-related quality of life

The UCP patients rated HRQOL including the four subscales of physical functioning, general health, vitality and mental health, measured by the SF 36. A significant gender

difference was seen in low physical functioning (compared with a normative population), reported by 26% of UCP men and 48% of UCP women (p=0.004) (Table 5, Paper II). When investigating correlations between HRQOL and pain intensity, a significant association was only found between pain intensity and physical functioning in men; pain intensity increased with decreasing physical functioning (p<0.05). In the correlations between HRQOL and the psychosocial factors, symptoms of depression and trait anxiety showed strong associations with vitality, mental health and general health in both genders (Table 6, Paper II).

Paper III

Differences between men and women with UCP and a reference group in terms of psychosocial factors such as symptoms of depression, trait anxiety, perceived stress at work and social interaction and HRQOL were analysed in Paper III.

Demographics and background characteristics

The results revealed that men with UCP had a significantly lower mean age (45.7 years) in comparison with men in the reference group (48.7 years) (p<0.01) (Table 2, Paper III). Furthermore, the percentage of immigrants was significantly higher among the UCP patients. The UCP patients were also significantly more sedentary during their leisure time and also had a significantly higher BMI than the reference group, in both men and women (p=0.01) (Tables 2 and 3, Paper III). Among UCP women, fewer had attended university than women in the reference group (25% versus 45%) (p=0.0001). The UCP women reported hypertension to a greater extent than the female referents (p<0.0001) and more of them were also current smokers (p=0.01) (Table 2, Paper III).

Psychosocial factors

Perceived stress at work, constant during the last year or the last five years, symptoms of depression and trait anxiety were reported significantly more frequently by the UCP patients compared with the reference group. Furthermore, after adjustments for age, smoking, hypertension and diabetes, these psychosocial factors were more frequent among the UCP men and women (Table 3, Paper III). After significant background variables and psychosocial factors were considered in a multivariate model, being an immigrant emerged as an independent risk factor for both men (OR 2.05 (1.15-3.66)) and women (OR 2.76 (1.56-4.86) (Table 4, Paper III).

Moreover, perceived stress at work was associated with an almost fourfold increase in risk among men (OR 3.94 (2.26-6.85), while no independent association for women was found. Having a sedentary lifestyle during leisure time was associated with a twofold increase in risk in men (OR 2.00 (1.06-3.79). Among women, symptoms of depression emerged as an independent risk factor (OR 2.09 (1.30-3.38), while a university education emerged as an independent protective factor (OR 0.47 (0.28-0.79) (Table 4, Paper III).

The patients with UCP were two to five times more likely to have low scores on their rated HRQOL in comparison with the reference group (Table 6, Paper III).

Paper IV

Trends in age-specific incidence of UCP in men and women

The incidence rates per 100 000 for men and women with UCP in the age groups 25-34, 35-44, 45-54, 55-64, and 65-74, were investigated between 1987 and 2004. The results showed that the incidence rates increased with increasing age, but, after 45 to 54 years among men and 55 to 64 years in women, no further increases were found. Among UCP men below the age of 55, the rates were higher than in women, while, above this age, the rates were more similar (Figures 1 and 2, Paper IV).

Trends in incidence rates for UCP, angina, and AMI

The results revealed that, among men and women aged 25-74, UCP and angina increased from the early 1990s (Figure 3, Paper IV). The incidence rates for angina peaked in around 1994 and then declined, while UCP continued to increase until about 2000 and then levelled out. AMI decreased throughout the period. At the ages of 75 to 84, the incidence trends for angina and AMI were similar in people aged 25-74, with a continuously declining trend after the early 1990s. In the older age group, the hospitalisation rates for UCP were much lower than those for angina or AMI and they also remained more stable throughout the period (Figure 4, Paper IV).

Characteristics and prognosis in patients hospitalised with UCP, angina and AMI

The number of patients with UCP in the younger age group was higher than that for angina and AMI (Table 1, Paper IV). The mean age for UCP patients was 53.6 years, for angina 62.7 years and for AMI 62.5 years. The one-year observed mortality rate for UCP was 10.4 per 1000, compared with 48.1 for angina and 142.8 for AMI. In the age group 75-84, the UCP patients accounted for only 14.7% of all patients with suspected ACS, while angina represented 40.8% and AMI 44.5%. The observed one-year mortality rate in UCP was substantial at 74.7 per 1000, compared with the age adjusted expected one-year mortality rate of 58.3 per 1000.

Prognosis in men and women hospitalised with UCP, 1987 to 2003

In the age group 25 to 74 the number of UCP males was higher than the corresponding number of females; 79 464 and 65 812 respectively (Table 2, Paper IV). The observed one year mortality rate per 1000 was among the UCP men 12.3, compared with 8.1 for the women, and the standardised mortality ratios (SMR) were 1.44 (95% CI 1.35-1.53) and 1.29 (95% CI 1.18-1.40) for men and women respectively. Women constituted 60.9% among the patients aged 75 to 84. After one year the observed mortality rate for men was 101.9, which can be compared with 57.2 for women. The ageadjusted expected one-year mortality rate for men was 75.6 to be compared with 47.3 for women. The results demonstrated that the UCP men had a significant increase in risk to die in the year following first hospitalisation, while the UCP women did not.

DISCUSSION

Discussion of findings

In this thesis, seen from a gender perspective, there were more similarities than differences in the descriptions of UCP. One of the most obvious gender differences was that UCP women reported more symptoms of depression and trait anxiety than UCP men, which is in accordance with Carmin et al. (2008) reporting that among patients with non-cardiac chest pain females more often than men presented anxiety-related symptoms. The UCP patients, both genders, suffered more than the reference group from psychosocial factors such as stress, symptoms of depression and trait anxiety. Another important finding was that more than a third of both UCP men and women were born outside Sweden and, compared with the reference group, the percentage of immigrants was significantly higher.

The majority of the patients with UCP were middle-aged. The UCP patients, both genders, were significantly more sedentary during their leisure time and had a higher BMI than the reference group. After a considerable increase from 1987 until about 2000, the incidence of first hospitalisation with a discharge diagnosis of UCP appeared to have levelled out. For angina, the incidence of first hospitalisation declined from about 1994, while the incidence for AMI declined throughout the period. The overall one-year observed mortality in UCP was lower compared with angina and AMI.

Pain perception

The UCP patients, both men and women, used words like "pressure" and "cramp" to describe their experiences of the chest pain, although some of the women described the pain more strongly than the men. Rating the worst chest pain intensity in the last 24 hours assessed by the POM (VAS 0-10) produced few gender differences, with a mean of 6.1 for males and 6.5 for females. Rating chest pain intensity retrospectively at the ED might be difficult, as the patients were then being cared for by the professionals and the investigators. Jerlock et al. (2006) found, for example, that UCP patients perceived greater pain intensity than those with IHD. In this thesis, pain quality assessed and described in predetermined sensory and affective word descriptors using the POM showed few gender differences. Both men and women selected the words "pressing" and "worrying" most frequently. It is, however, important to remember that pain might be described and perceived differences, as half of both men and women described their chest pain as "intermittent" and half as "continuous".

Pain localisation was reported mostly in the left side region by both genders, possibly causing difficulty differentiating UCP from IHD. Jerlock et al. (2006) found differences in pain location between UCP patients and those with IHD; UCP patients reported significantly more pain in the front centre left region than the patients with IHD. In overall terms, the findings in this thesis showed few gender differences due to chest pain perception. These findings do not always agree with previous studies, showing differences by gender in chest pain perception and diagnosis (Miller, 2002; Granot et al., 2004; Chen et al., 2005; Nau et al., 2005; Omran & Al-Hassan, 2006).

According to Vodopiutz et al. (2002), when studying cause and gender-specific differences in chest pain patients, the differences in pain might be due to the self-presentation and underdiagnosis of females with chest pain. Even if the perceived pain intensity was not extremely high, several of the UCP patients said that the chest pain affected their daily life in a negative way. Different consequences of chest pain also appeared from the descriptions of living with UCP; they included a fear of dying. In their descriptions of UCP, several of the patients used metaphors, corroborating Skott (2002) "using metaphors is a way of understanding one kind of experience in terms of another more familiar and well known experience" (p. 230), i.e. in an understandable context.

Several of the UCP patients also worried about what was actually causing their chest pain and stated that they had not been given any clear explanation or medical diagnosis by the physician, which increased their worry and uncertainty. Previous research has indicated the importance of communication and empathy on the part of the physician towards patients and their anxiety when suffering from medically unexplained symptoms (Epstein et al., 2006; Epstein et al., 2007).

Psychosocial factors

Stress

In our society in the western world, we appear to live our lives overloaded with the desire to attain goals defined "as the good life", sometimes leading to lives filled with stress and dissatisfaction. The UCP patients, both the men and women, perceived their lives as stressful. Stress at home and stress at work emerged from several of the descriptions by the patients when they talked about their daily life. Perceived constant stress at work during the last year was also frequently reported by almost half of both UCP men and women, although, not surprisingly, the women experienced stress at home to a greater extent than the men. According to Schnall (1990), job strain/stress occurs when an individual has a limited opportunity to make decisions at work related to high psychological demands (Schnall et al., 1990) and this might end in psychological strain with an increased risk of cardiovascular diseases, sleeping problems, anxiety and depression (Kristensen, 1996).

One interesting and highly relevant question in relation to this issue could be whether the experienced stress depends on the UCP patients' life and/or work situation or whether this group of patients has difficulty coping with stress in general. In addition, how does the stress, sometimes up to five years of constant stress, affect their body and mind? Previous research has indicated that there is a relationship between health, especially mental health, health care use and stress at work (Manning et al., 1996). Previous studies have also reported differences between the sexes in perceiving stress. Role conflicts and job overload have been reported to be stressful for women, whereas men responded more to stress at work, stress causing different psychosomatic symptoms and cardiovascular diseases (Lundberg, 1996).

Depression, anxiety and panic disorder

In accordance with Sadock et al. (2007), indicating a higher prevalence of depression and anxiety in females, the findings in this thesis demonstrated that symptoms of de-

pression and trait anxiety were significantly more frequently experienced by the UCP women than the men, findings which have also been made in women suffering from angina pectoris (Sundel et al., 2007). Compared with the reference group, the UCP patients, both sexes, reported significantly more symptoms of depression and trait anxiety. The UCP patients' perceived symptoms of depression and trait anxiety could be related in part to difficulties associated with not being born in Sweden. Corroborating Eisenberg and Kleinman (1981) and Kirmayer and Young (1998), cultural and subcultural aspects have to be considered when attempting to understand illness of both a somatic and psychiatric nature. The way the patient expresses and talks about different symptoms must always be considered and interpreted from the knowledge of how pain can be expressed in various cultures, for example, a knowledge all professionals should have. Moreover, in line with previous knowledge regarding the associations between psychosomatic symptoms and IHD (Marusic & Gudionsson, 1999; Rozanski et al., 1999; Fiscella et al., 2007; Vural et al., 2007), this thesis indicated connections between psychosocial symptoms and perceived UCP, which must be taken into account when taking the UCP patients' clinical history at the ED.

In a critical analysis of the conditioning for developing cardiophobia, recurrent chest pain with no pathology, Zvolensky et al. (2008) stressed that cardiophobia can be found in a small percentage of individuals who are anxious about having a heart attack, for example, associated with bodily symptoms that could be related to the heart.

Suffering panic disorder, previously or currently, associated with UCP, was described by several patients in Paper I. Both UCP men and women admitted that they suffered repeatedly from panic, which could complicate diagnosing UCP, in accordance with earlier studies indicating difficulties in diagnosing and distinguishing panic disorder and non-cardiac chest pain (Dammen et al., 1999; Bringager et al., 2004; Dammen et al., 2004). One most interesting question is, however, whether panic disorder could be manifested as UCP. Or does suffering UCP generate panic, as well as symptoms of depression and anxiety? What are actually cause and effect? Correctly diagnosing panic disorder in UCP patients is essential, as Bull Bringager et al. (2008) found, in a long-term follow-up study of chest pain patients with or without panic disorder, that the patients suffering panic disorder reported higher scores for pain intensity, anxiety, depression and reduced HRQOL than the patients without panic disorder.

Social interactions

The findings showed that the UCP patients lived their lives with a sometimes weak social network. Several of both the males and the females said that they had hardly any time for social contact, except with the family. On the other hand, some of the men, who were single parents, said that being with their children was their most important role in life, findings that agree with the previous study by Peat et al. (2004). In our study, one single man said that he was totally alone and had absolutely nobody to talk to. In accordance with previous findings when studying men in pain, our study revealed that some of the men did not have much energy for their social life (Paulson et al., 2002), even if several of the participants expressed a pronounced need to talk but felt that they could not trouble their relatives by talking about worries and fear due to UCP. Few of the participants felt that the professionals had time to confirm their

worries. Even if the conditions within health care provide few opportunities for just talking, this group of patients really needs someone, such as an expert nurse, to share and confirm their suffering. The importance of listening and communicating with patients is crucial for the outcome of care and this has also been demonstrated in other health care settings (Kjellgren et al., 1998).

Health-related quality of life

The UCP patients, both genders, estimated their HRQOL as relatively low, lower than the reference group. It was, however, interesting and noteworthy to find that chest pain intensity was not significantly associated with HRQOL, apart from physical functioning in men. So why did the UCP patients estimate their HRQOL lower than their referents? Might these men and women have something in common that negatively influences their lives? As described above, the UCP patients, and the women in particular, reported more symptoms of depression and trait anxiety than their referents and this probably influenced their perceived HRQOL. Another reason for the low HRQOL ratings might be that the UCP patients, both genders, reported higher co-morbidity than the reference group. The patients had a significantly higher BMI, for example, and the females reported hypertension and were current smokers more frequently than their referents. Remembering that HRQOL measures the person's subjective rating of current health status (Shumaker & Berzon, 1995), and the UCP patients assessed their HRQOL when suffering UCP at an ED or as in-patients on a medical ward, the results of the rated HRQOL were not unexpected.

Self-efficacy – human capabilities

Self-efficacy theory expresses the variety of human capabilities (Bandura, 1997). Efficacy convictions compromise both control of action and the self-regulation of thoughts, affective and physiological states and motivation. However, effective personal functioning is not just a matter of being aware of what to do and being motivated to do it. Perceived self-efficacy is what you think you can do with the skills you have in different circumstances in life. Bandura (1997) says that people's beliefs in their own capability to change harmful health habits and that physical activity as a form of health promotion, for example, is a protective factor against various chronic diseases. Maddux (1995) states that research has shown that low self-efficacy is characteristic in conditions such as depression, anxiety problems and substance abuse.

The results in this thesis suggest that patients suffering UCP have better one-year survival than those with angina and AMI. In spite of this, the UCP patients perceived more symptoms of depression, trait anxiety and stress than the reference group. When describing their chest pain, the most frequently used affective word was "worrying". So, even if they "survived", they appear to live their lives with some worry and negative emotions. Bandura's advice is to believe in your own capability to change what it is not good and healthy in life. However, it is not easy to change unhealthy habits. According to Bandura (1997), health promotion, such as physical activity, could be a protective factor and this is important information for UCP patients reporting a sedentary lifestyle during their leisure time. The professionals must support the UCP patients in strengthening their belief in their own self-efficacy to cope with stressful events in life.

Methodological considerations

In this thesis, both qualitative and quantitative methods have been used to obtain a broader understanding of the UCP patients' conditions. The validity may be improved by the use of combination of research methods (Greenhalgh & Taylor, 1997). Evidence was sought from different sources and by different methods. We obtained a high similarity in results between the studies, e.g. regarding age and immigrants.

According to Polit and Beck (2004), the investigators' focus in a qualitative study should be, in a specific context, a comprehensive understanding of the studied phenomenon. Paper I was a qualitative descriptive study designed to obtain a deeper understanding of how UCP can be experienced and may affect the patients' daily life. It is, however, important to remember that the difficulties involved in assessing and elucidating pain may possibly be perceived and described differently, depending on the patients' culture and ethnicity. Attention also needs to be paid to the large number of immigrants who were included and did not have Swedish as their mother tongue. The majority of the interviews were carried out at the participants' homes, several were conducted on the medical ward after receiving a diagnosis of UCP and two were conducted at the participants' workplace. The place at which the interviews were conducted could have had some influence on the content of the narratives, even if it was essential that the participants felt comfortable in the interview situation. The interviews were held after the data collection in Paper II was completed and it therefore probably had no effect on the investigators' interpretation of the interviews, as the data analyses in Paper II had not yet been performed.

The data in Papers I, II and III were collected at the same hospital in Gothenburg serving inhabitants from the eastern part of the city and this could possibly have affected the results, including the large number of immigrants referred to the ED in question. However, after an investigation comparing the place of birth of the inhabitants who were referred to the remaining EDs in Gothenburg, no obvious differences in immigrant status were found between them.

Paper II was a quantitative cross-sectional study, investigating differences in pain characteristics, psychosocial factors and health-related quality of life by gender. The patients estimated their chest pain using the POM (Gaston-Johansson, 1996), which tended to be a comprehensive way of assessing pain, as both sensory and affective word descriptors were included in the measurement. Somehow it was not always easy for the patients to differentiate the various words from another and evaluate them and the fact that several of the included patients did not have Swedish as their mother tongue also had an impact. The questionnaire was personally presented by the investigators and, in line with Polit and Beck (2004), this usually has a positive effect on the response rates. The questionnaire comprised 184 items and, in addition to demographics and biomedical risk factors, it consisted of several established, validated scales which made it possible to compare our results with those of other studies comprising patients with similar illnesses and diseases. All the scales were also selected to match the scales used in the INTERGENE study. In Paper II, only four of the eight subscales in the SF 36 were included; physical functioning, general health, vitality and mental health. The reason for excluding the remaining four scales was the risk of interfering with other scales included in the questionnaire.

Psychosocial factors and HRQOL in patients with UCP and the reference group were compared in Paper III. Even if there were a large number of drop-outs from the IN-TERGENE study, in line with other large population studies, the findings are most valuable. Paper IV was a register study in which the source of errors always has to be taken into account. To reduce the risk of Type I errors (Altman, 1991), a significance level of 1% was chosen, when testing the hypotheses of the items in the question-naire.

Since the sample is fairly large the risk of rejecting differences of importance is low. Power calculations on observed results reveal that OR estimates about 2.5 lie well above 0.95. It is therefore safe to state that true OR rates above 2.0 can be secured with satisfactory power, corresponding to a prevalence twice as high as that of the reference group.

CONCLUSIONS

The men and women suffering UCP were generally middle-aged and more than a third of both genders were born outside Sweden. The UCP patients talked about a daily life influenced by physical and psychological limitations due to the chest pain. Feelings of panic and fear of death in connection with UCP were also described. The descriptions and consequences of UCP had more similarities than differences in both men and women and no gender differences regarding chest pain intensity were seen. Words like "pressure" and "cramp" were used to describe the UCP, with few gender differences.

The results revealed further significant associations between pain intensity and current smoking in men (p<0.01) and pain intensity and increasing age in women (p<0.05). Chest pain intensity was not significantly associated with the UCP patients' reported HRQOL, apart from physical functioning in men (p<0.05), but it was rated lower than the reference group of both UCP men and women. The women with UCP presented more symptoms of depression and trait anxiety than the men, while stress at work was reported more frequently by the UCP men. Mental strain in marriage/cohabitation and low social integration were only significant risk factors among women. Compared with the reference group, the UCP patients, both genders, perceived more stress at work, symptoms of depression and trait anxiety. Gender differences in physical activity during leisure time were reported, as more UCP males than females were physically active, although the UCP patients, both men and women, had a significantly higher BMI and lower alcohol consumption/week than the reference group.

After a considerable increase from 1987 until about 2000, the incidence of first hospitalisation with a discharge diagnosis of UCP appears to have stabilised, while hospitalisations for angina and AMI have continuously declined. The overall one-year observed mortality in UCP was lower compared with that for angina and AMI. Between 1997 and 2003 the one-year mortality among men with UCP was elevated by one third, whereas women with UCP had no significant increase.

CLINICAL IMPLICATIONS

The findings in this thesis can be useful and help us to understand that symptoms of depression, trait anxiety, stress at work and social interaction could influence the chest pain in patients suffering from UCP. When taking the UCP patients' clinical history at the ED and in assessments in clinical settings, associations between psychosocial symptoms and perceived UCP must therefore be considered.

The results from the interviews have also extended our knowledge of the way communication and interaction between the patient and the professionals can be used in a therapeutic manner, as several of the UCP patients talked about their pronounced need to narrate and be confirmed in their suffering. For this reason, understanding and empathy on the part of the professionals are also important, as the UCP patients worried about what was in fact causing their chest pain.

The large number of immigrants among the patients with UCP will impose new demands on the professionals' knowledge of the way symptoms of illness and disease may be described in different cultures. When needed, an interpreter should be called in to the consultations with the UCP patients who do not have Swedish as their mother tongue.

Lifestyle counselling for the UCP patients reporting a sedentary lifestyle during their leisure time and stress at work could be very important. It might also be interesting to create specific patient groups within primary health care, offering UCP patients learning situations, i.e. education and the opportunity to share experiences and support each other.

FURTHER RESEARCH

Further research should focus on clinically establishing and following up suggested lifestyle counselling with an inter-disciplinary and cultural perspective, taking account of the large number of immigrants among UCP patients.

In order to offer adequate care and treatment to UCP patients, guidelines influenced by the biopsychosocial model, for assessments of psychosocial factors and HRQOL associated with UCP, should be developed and evaluated.

Further research should also aim to find more effective ways of identifying whether there are any organic causes of UCP and investigating the causes of death and impact of age and gender on the mortality trends among patients suffering from UCP.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Bröstsmärta är en vanlig orsak till att patienter söker vård akut. Ett stort antal av dessa patienter får diagnosen oförklarad bröstsmärta dvs. bröstsmärtan kan inte förklaras av biomedicinska faktorer som hjärtsjukdom eller annan organisk sjukdom. En stor del av dessa patienter söker vård vid upprepade tillfällen och eftersom orsaken till bröstsmärtan inte är känd kan det vara svårt att erbjuda adekvat vård. Oförklarad bröstsmärta livskvalitet utan också stora kostnader för samhället. Ringa forskning har bedrivits inom detta område och kunskapen om eventuella faktorer som kan påverka den oförklarade bröstsmärtan är begränsad.

Det övergripande syftet med avhandlingen var att beskriva och analysera upplevda symptom hos patienter med oförklarad bröstsmärta genom att dels undersöka skillnader mellan män och kvinnor vad gäller bröstsmärta, psykosociala faktorer och hälsorelaterad livskvalitet och dels jämföra med en referensgrupp. Vidare var syftet att studera utveckling och prognos av patienter med oförklarad bröstsmärta över tid, i jämförelse med patienter med kärlkramp och hjärtinfarkt.

Avhandlingen består av fyra studier där både kvalitativa och kvantitativa metoder har använts. I studie I intervjuades 20 patienter (11 män och 9 kvinnor) om sin bröstsmärta och hur den påverkade deras dagliga liv. Studie II var en beskrivande studie där 179 patienter (101 män och 78 kvinnor), som sökt vård på en akutmottagning i Göteborg, skattade sin svåraste bröstsmärta under de senaste 24 timmarna med ett smärtbedömningsinstrument, Pain-O-Meter. Patienterna fyllde också i ett frågeformulär som innefattade frågor om demografiska och psykosociala faktorer samt hälsorelaterad livskvalitet. Studie III var en jämförande studie omfattande 231 patienter med oförklarad bröstsmärta (127 män och 104 kvinnor) och en referensgrupp bestående av 1069 individer (490 män och 579 kvinnor) från populationsstudien INTERGENE. Studie IV var en register studie med data från socialstyrelsens slutenvårdsregister omfattande 559 879 patienter.

Resultaten visade att männen och kvinnorna med oförklarad bröstsmärta till större delen var medelålders. Mer än en tredjedel av båda könen var födda utanför Sverige. Patienterna berättade i Studie I att bröstsmärtan påverkade deras dagliga liv negativt genom att den medförde begränsningar i livet. I sina beskrivningar om hur bröstsmärtan upplevdes fanns mer likheter än olikheter mellan könen. I Studie II beskrev framförallt männen att de upplevde sitt arbete stressigt medan kvinnorna upplevde mer symtom av nedstämdhet och ångest. Kvinnorna beskrev också att de upplevde mer problem i äktenskapet/samboförhållandet än vad männen gjorde. I jämförelser med referensgruppen (Studie III) upplevde patienterna, både männen och kvinnorna, fler symptom av nedstämdhet och ångest och stress i arbetet. Trots att den hälsorelaterade livskvaliteten hos patienterna inte påverkades av bröstsmärtans intensitet skattade båda könen den lägre än vad referensgruppen gjorde. De manliga patienterna var mer fysiskt aktiva på fritiden än kvinnorna (Studie II) men jämfört med referensgruppen hade både männen och kvinnorna i patientgruppen en mer stillasittande livsstil. Register studien (Studie IV) visade att från 1987 och fram till 2000 ökade antalet patienter

med diagnosen oförklarad bröstsmärta, därefter har ökningen planat ut. Antalet patienter med kärlkramp ökade fram till 1994 och har sedan minskat, medan antalet patienter med hjärtinfarkt har minskat under hela den undersökta perioden. Dödligheten ett år efter insjuknandet var lägre hos patienter med oförklarad bröstsmärta jämfört med patienter som insjuknat i kärlkramp eller hjärtinfarkt. Ett år efter insjuknandet i oförklarad bröstsmärta under åren 1997-2003 var dödligheten bland männen högre än förväntat, medan kvinnorna inte hade någon ökad risk för död.

Sammanfattningsvis var den oförklarade bröstsmärtan relaterad till symptom som påverkade patienterna på flera sätt. Könsskillnaderna var relativt få och dödligheten efter ett år låg. Avhandlingen visar på betydelsen av förbättrad kunskap och förståelse av de symptom som patienter med oförklarad bröstsmärta uppvisar för att kunna ge en mer individualiserad vård.

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