Management of COPD and chronic heart disease in primary health care

Dedication
To my dear parents, Henk and Miep,
who gave me all the tools to succeed and be happy in life

Örebro Studies in Medicine 269

MAAIKE GIEZEMAN

Management of chronic obstructive pulmonary disease and chronic heart disease in primary health care

Guidelines, patients and comorbidity

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Abstract

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The overall aim of this compilation thesis was to explore different aspects of the management of patients with chronic obstructive pulmonary disease (COPD) and heart disease in primary health care: guideline adherence in chronic heart failure (CHF) management (I); comparing patients with COPD and heart failure, and factors associated with the patients' exercise self-efficacy (II); and the influence of comorbid heart disease in COPD over time (III–IV).

Materials and methods: Cross-sectional data from primary health care: 155 patients with heart failure (I) and 150 with COPD and/or heart failure (II). Longitudinal data from patients with COPD from 2005 through 2012 (III) and 2019 (IV), based on questionnaires, medical records, and national registers.

Results: (I) Over 80% of the heart failure patients had received relevant laboratory tests and echocardiography. Recommended medication was given to most of the patients, but only a few achieved target doses. Contact with a hospital heart failure clinic was associated with better self-care behavior. (II) Patients with COPD or heart failure had similar exercise self-efficacy, symptoms, functional capacity, and health status. Exercise self-efficacy was associated with symptoms, but not with the diagnosed disease. (III) COPD with comorbid heart disease was associated with a lower health status and higher level of dyspnea but did not accelerate the worsening over time. (IV) Comorbid heart disease was associated with increased hospitalization and mortality, not for respiratory disease, but mainly for cardiovascular and other causes.

Conclusions: Adherence to guidelines for CHF in primary health care is suboptimal, particularly regarding medication target dosage and patient education. It seems more relevant to consider the symptom level than the specific diagnosis when forming self-management groups to increase exercise self-efficacy. In COPD management in primary health care, it is important to recognize and treat heart disease.

Keywords: COPD, chronic heart failure, heart disease, patient outcomes, exercise self-efficacy, comorbidity, primary health care, cohort study

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List of publications

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

I Giezeman M, Arne M, Theander K. Adherence to guidelines in patients with chronic heart failure in primary health care. Scand J Prim Health Care. 2017;35(4):336–343. *

II Giezeman M, Theander K, Zakrisson AB, Sundh J, Hasselgren M. Exploration of the feasibility to combine patients with chronic obstructive pulmonary disease and chronic heart failure in self-management groups with focus on exercise self-efficacy. Scand J Prim Health Care. 2022;40(2):208–216. *

III Giezeman M, Hasselgren M, Lisspers K, Ställberg B, Montgomery S, Janson C, Sundh J. Influence of comorbid heart disease on dyspnea and health status in patients with COPD: a cohort study. Int J Chron Obstruct Pulmon Dis. 2018;13:3857–3865. **

IV Giezeman M, Sundh J, Athlin Å, Lisspers K, Ställberg B, Janson C, Montgomery C, Kisiel MA, Nager A, Sandelowsky H, Hasselgren M. Comorbid heart disease in patients with COPD is associated with increased hospitalization and mortality: a 15-year follow-up. Accepted for publication in Int J Chron Obstruct Pulmon Dis.

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Abbreviations

BB	Beta blocker
BNP	B-type natriuretic peptide
CAT	COPD assessment test
CCQ	Clinical COPD questionnaire
CHF	Chronic heart failure
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
ECG	Electrocardiogram
EF	Left ventricular ejection fraction
EHFScBS	European heart failure self-care behaviour scale
ESC	European society of cardiology
ESES	Exercise self-efficacy scale
EQ-5D-5L	EuroQol group questionnaire; 5 dimensions and 5 levels
FEV_1	Forced expiratory volume in one second
FEV_1%pred	FEV_1 as percentage of the expected value
FVC	Forced vital capacity
GOLD	Global initiative for obstructive pulmonary disease
GP	General practitioner
HAD	Hospital anxiety and depression scale
HFrEF	Heart failure with reduced ejection fraction
HFmrEF	Heart failure with moderately reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
IQR	Interquartile range
mMRC	Modified medical research council dyspnea scale
MRA	Mineralocorticoidreceptor antagonist
NT-proBNP	N-terminal proBNP
PHCC	Primary health care center
RAAS	Renin angiotensin aldosterone system
RASi	Inhibitor of the renin angiotensin system
SD	Standard deviation
TTE	Transthoracic echocardiography
VAS	Visual analog scale

Introduction

Over the last two centuries, living standards and general health have increased drastically. There has been great progress in medical and technical abilities to prevent, detect, and cure diseases. As a result, more people live to greater ages, but often with one or several chronic diseases. This has placed an increased economic burden on society and poses a challenge to the health-care system organization and health-care professionals because of the complexity of managing this patient population [1]. The World Health Organization (WHO) considers primary health care to be a cornerstone of sustainable health-care systems, where individuals are empowered to take charge of their own health and health care is delivered in the most efficient and effective way [2].

In many health-care systems in Europe, general practice is the key provider of primary health care. Care is often delivered by a multiprofessional team, coordinated by general practitioners (GPs). In 2011, WONCA Europe published a definition of general practice describing eleven essential characteristics of the discipline and translating them into six core competencies: primary care management, person-centered care, specific problem-solving skills, a comprehensive approach, community orientation, and holistic modeling [3]. In 2020 the Nordic Federation of General Practice published the core values and principles of Nordic general practice [4]. Among others, a person-centered approach is emphasized by both organizations as an important characteristic of good general practice. A person-centered approach means that the focus is on the patient having the disease, and not just on the disease itself. An important part of care management is to understand the patient's beliefs, worries, and hopes and how the illness influences the patient's life. This also makes a "comprehensive approach" necessary, an approach in which multiple complaints and pathologies are managed simultaneously. This requires that the GP should be updated on the latest recommendations for the evaluation and treatment of the most common diseases and should understand how comorbidity influences the patient's daily life and prognosis. The Nordic Federation of General Practice also stresses that it is the GP's task to encourage progress toward health, helping patients to understand their own health, confront and manage their limitations, and improve and maintain their wellbeing.

This thesis covers several aspects of the management of chronic obstructive pulmonary disease (COPD) and chronic heart disease. These are large

patient groups and comorbidity of COPD and heart disease is common. The focus will be on guideline adherence in the management of chronic heart failure (CHF), patient outcomes in COPD and CHF, and the influence of comorbid heart disease on patient outcomes in COPD over time.

Background

Epidemiology and characteristics of COPD and heart disease

COPD

COPD is a chronic progressive lung disease characterized by chronic airway obstruction due to bronchiolitis and emphysema. It has a prevalence of approximately 10% in the total population over 40 years and increases with age [5,6]. In 2019 WHO estimated COPD to be the third leading cause of death, surpassed only by ischemic heart disease and stroke [7]. In Northern Europe, COPD is mainly caused by exposure to tobacco smoke but can also be caused by occupational exposure and outdoor air pollution from industry and traffic [8]. The lung damage in COPD is irreversible and slowly progressive and has a negative impact on the patient's quality of life. The most important clinical problems are exacerbation periods, characterized by increased dyspnea, cough, and sputum volume, that need medical treatment and can require hospitalization. Each exacerbation may cause a permanent decline in lung function, and once exacerbations start, the patient has a high risk of dying within a few years [9,10].

Chronic heart disease

This thesis studies CHF and chronic ischemic heart disease, which are jointly referred to as chronic heart disease when both are involved. Also, when discussing comorbid heart disease, these two disease groups are being referred to.

Chronic heart failure

Chronic heart failure (CHF) is mainly a disease of the elderly, often caused by a long history of uncontrolled hypertension or loss of myocardium due to ischemic heart disease [11]. CHF is associated with high rates of morbidity and mortality and high costs to society, mainly because of frequent hospitalizations [12,13]. In Sweden the prevalence is about 2% in the general population, but 10% in those aged 70 years and older [14]. The CHF patients managed in primary health care are often older and have a preserved left ventricular ejection fraction (EF) [15,16].

CHF is a complex clinical syndrome resulting from a structural or functional cardiac disorder causing insufficient circulation, which activates the renin-angiotensin-aldosterone system (RAAS). When the left ventricle of

the heart is stretched, the myocardium produces B-type natriuretic peptides, which are used as a biomarker of heart failure [17]. Typical symptoms of heart failure are dyspnea, cough, and fatigue, and typical clinical signs are pulmonary crackles, swollen ankles, and elevated jugular venous pressure.

Chronic ischemic heart disease

Ischemic heart disease leads the top 10 causes of death worldwide [7]. Since mortality caused by acute ischemic heart disease is decreasing due to improving preventive and therapeutic measures, the number of patients living with chronic ischemic heart disease is growing and the prevalence in the world population is estimated to be 1.7% [18]. The prevalence of angina in population-based studies is estimated to be 10–14% in patients over 65 years old [19].

Patients with chronic ischemic heart disease have a plaque-related obstruction of the coronary arteries. This can lead to episodes of reversible myocardial ischemia, usually induced by exercise or stress, leading to chest pain (angina) or dyspnea. Chronic ischemic heart disease also includes patients in the stabilized phases that follow an acute coronary event or who underwent revascularization therapy. These patients may be completely symptomless [20]. Secondary cardiovascular risk management is an important task of primary health care [21,22].

Guidelines

Guidelines are general recommendations for how to diagnose, treat, and follow up specific diseases or disease groups in health care and are often issued by medical associations or governments. Guidelines are regularly updated and based on the latest evidence from medical research or on a consensus of leading expects in a specific area. A short summary of the guidelines for COPD and CHF relevant to management in primary health care is given below.

COPD guidelines

The Global Initiative for Obstructive Pulmonary disease (GOLD) has issued recommendations for the diagnosis and treatment of COPD [8]. The national guidelines issued by the Swedish National Board of Health and Welfare and the Swedish Medical Products Agency are based on the same evidence

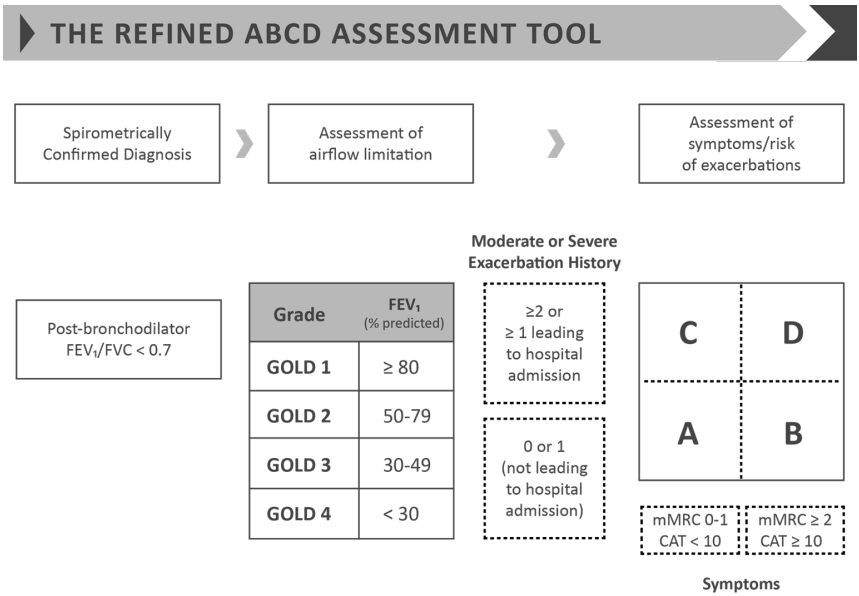

Figure 1. © 2020, Global Initiative for Chronic Obstructive Lung Disease: the refined ABCD assessment tool [25].

but adapted to the Swedish system; however, these guidelines are not updated annually and are not always up to date [23,24]. For a diagnosis of COPD, spirometry has to confirm chronic obstruction of the airways, using a value of less than 0.70 for the ratio of the post-bronchodilator forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC). Until 2011 the severity of the disease was determined only by airflow limitation, expressed as the forced expiratory volume in one second as a percentage of the predicted value (FEV1 % pred). More recently, symptom or health status evaluation and exacerbation frequency were also included to assess COPD severity. Today a combined COPD assessment is recommended, with COPD first being classified into four spirometric stages of airflow limitation followed by severity grading in groups A–D based on exacerbation frequency and symptoms measured by the modified Medical Research Council dyspnea scale (mMRC) or health status measured by the COPD Assessment Test (CAT) (Figure 1) [25]. The CAT was developed in 2009, and until recently another health status measure, the

Clinical COPD Questionnaire (CCQ), was also recommended in the GOLD guidelines.

In primary health care, patients with COPD are mainly treated with inhaled beta-agonists, long-acting muscarinic antagonists, inhaled corticosteroids, or a combination of these, depending on symptoms, health status, and exacerbation frequency.

Medication is important for a patient with COPD, but even more important is smoking cessation and a healthy lifestyle as a whole. An important part of self-management is to perform exercise training [8].

Chronic heart failure guidelines

The European Society of Cardiology (ESC) issued guidelines in 2012 for the evaluation and pharmacological and non-pharmacological treatment of CHF [26]. Treatment options for heart failure have improved since that time, and the ESC guidelines were updated in 2016 and 2021 with a new classification system and new treatment options [11,27]. There are also Swedish guidelines from 2006 and 2018 and, in 2021, a published standardized care program from the national system of knowledge-driven management within Swedish health care [28-30].

The guidelines advocate that electrocardiography (ECG), and level of natriuretic peptides should be assessed when CHF is suspected based on medical history, symptoms, and signs. If either is abnormal, transthoracic echocardiography must be performed to confirm the diagnosis and to assess the left ventricle EF, structural changes, and diastolic function of the heart (Figure 2). The guidelines also recommend tests for the exclusion of other conditions, evaluation of treatable causes of CHF, and for the follow-up of treatment.

The classification of CHF is based on the EF. In 2012 the terms "heart failure with reduced ejection fraction" (HFrEF) and "heart failure with preserved ejection fraction" (HFpEF) were introduced, but without a strict limit for the EF to distinguish between the two [26]. Since 2016 three classes of heart failure have been recognized based on the left ventricle function: heart failure with reduced EF of <40% (HFrEF), heart failure with preserved EF of ≥50% (HFpEF), and the intermediate group, heart failure with a mid-range EF of 40–49% (HFmrEF) [27]. In 2021 the abbreviation HFmrEF was changed to represent "heart failure with mildly reduced ejection fraction" and the range was altered from 41-49% [11].

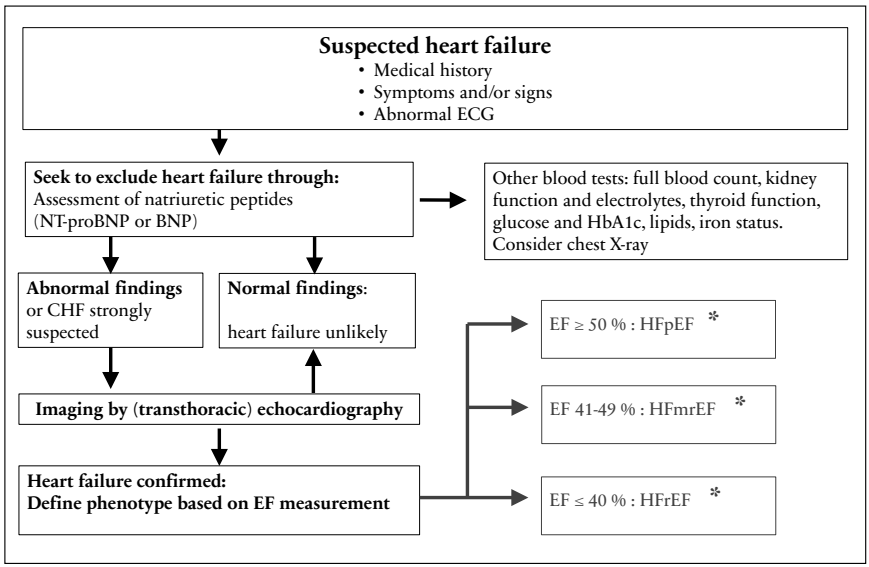

*Figure 2. Diagnostic algorithm for heart failure. * Heart failure phenotypes according to the ESC guidelines published in 2021 [11].*

The recommendations for pharmacological treatment differ between the three heart failure groups, but diuretics are important for all types of heart failure to reduce fluid overload.

In patients with HFrEF there is solid evidence that up-titration of renin angiotensin system inhibitors (RASi) and beta-blockers (BB) to a target dose decreases mortality, symptoms, and hospitalizations and improves health status. The guidelines up to 2021 recommend starting the treatment with these two medication groups, and if the patient remains symptomatic, to add a mineralocorticoid receptor antagonist (MRA). In the ESC guidelines from 2021, sodium-glucose cotransporter-2 (SGLT2) inhibitors were added to the standard pharmacological treatment of HFrEF, and treatment with all four medication groups has to be started within four weeks of suspecting the diagnosis. If the patient remains symptomatic, the RASi can be replaced with an angiotensin receptor neprilysin inhibitor (ARNI).

In patients with HFpEF, there were until recently no drugs with certain prognostic benefit, so treatment strategies were symptom focused and include titrating diuretics to the fluid status of the patient, adequate blood

pressure control, and control of heart rate. Since 2022 there is evidence that SGLT2 inhibitors also are beneficial for patients with HFpEF.

Up to 2021, it was recommended that patients with HFmrEF should be treated as HFpEF patients; the newest recommendations permit treating HFmrEF as HFrEF.

The guidelines emphasize that it is important that patients with CHF understand their condition and actively engage in self-care management. Patients should be made aware of the role of salt and encouraged to avoid overuse, of the importance of ensuring adequate hydration and a healthy diet, and of the importance of regular exercise to increase functional capacity. For patients with more severe HF, daily weighing and fluid restriction are crucial.

Comorbidity

Heart disease is a common comorbidity in patients with COPD [31-33]. COPD patients have a two to five times higher risk of developing heart disease [34]. For ischemic heart disease, the prevalence is 5–60% and for CHF, the prevalence is 7–31% in patients with COPD [31-35]. The observed association between COPD and ischemic heart disease can partly be explained by shared risk factors such as smoking, age, and inactivity. However, it is also thought that a systemic inflammatory process related to COPD independently increases the risk of heart disease [36,37].

When a patient is suspected of having a chronic heart disease or COPD, the other disease group has to be considered in the differential diagnosis. CHF is often unrecognized in patients with COPD and airflow limitation can be the cause of chest tightness in patients evaluated for angina [35,38].

The common coexistence of COPD and heart disease has important implications from a clinical standpoint. COPD has been shown to trigger incident cardiovascular events and worsen existing heart disease [39,40]. Conversely, it has also been shown that heart disease is associated with more COPD exacerbations [41-43]. Several cross-sectional studies have demonstrated increased risks of hospitalization and mortality and lower quality of life among patients having both chronic conditions [44-50]. However, not all studies have found an increased risk of hospitalization and mortality in patients with COPD and comorbid heart disease [51,52].

Patient outcomes

In the management of COPD and chronic heart disease, the correct diagnosis and objective measurement of disease are important, as described above. The patients need to know about and understand the nature of their disease. But in daily life, the patients mainly experience the consequences of the disease as symptoms and limitations in performing desired activities. The patients must adjust their lifestyles, either because of the symptoms and limitations or to prevent deterioration of the disease. Therefore, in management, it also is important to consider patient-related outcomes. Some outcomes can be measured objectively, such as mortality and hospitalization. When outcomes cannot be measured objectively, patient-reported outcomes can be used instead; standardized and validated measuring instruments, mostly presented as written questionnaires, have been developed for this.

Health status

Improving quality of life is an important goal in the management of COPD and chronic heart disease. Quality of life has been described as "a holistic, self-determined valuation of satisfaction with issues important to the patient" and can be influenced by social and economic factors and by health [53]. To describe the impact of disease on a patient's wellbeing, the term health-related quality of life is used [53]. Health status includes the subjective impact of a disease on physical, psychological, and social performance and on health-related quality of life [54]. Although not entirely the same, health-related quality of life and health status are often used interchangeably. It is suggested that the term health-related quality of life is better reserved for describing clinical outcome as experienced by the patient, and health status as the marker used to measure that outcome [55].

Symptoms

Symptoms are defined as "a patient's perception of an abnormal physical, emotional or cognitive state" [56]. Symptoms cannot be seen and do not show up on medical tests but have to be reported by the patient [57]. Patients with COPD and CHF have many symptoms in common. Besides the cardinal symptoms of dyspnea and fatigue, even pain and depressive and anxiety symptoms are common in patients with these diseases [58].

Functional capacity

In the literature there are conflicting definitions describing functional status [59]. The definition can be broad, including the patient's ability to participate in activities in the physical, social, cognitive, psychological, and spiritual domains, or it can be narrower and describe the patient's ability to participate in activities of daily life, and in this way mainly focus on the physical domain. The same applies to the definition of functional capacity, which is described as "an individual's full potential to participate in their lives in all domains" or mainly as functional "exercise" capacity [60,61]. In this thesis the narrower definitions are used.

Self-care behavior

WHO defines self-care as "the ability of individuals, families and communities to promote health, prevent disease, maintain health, and to cope with illness and disability with or without the support of a healthcare provider" [62]. For patients with COPD or heart disease, this means that the patients are able to self-manage their symptoms and illness in their daily lives. This includes adherence to both non-pharmacological and pharmacological treatment regimens. Besides giving the patients more control over their own lives, good self-care behavior can reduce the need for professional help and hospitalization [63,64].

An important part of the self-management of both COPD and CHF is to perform exercise training [8,11]. Studies have shown that exercise training reduces and prevents muscle deconditioning, improves patient health, and decreases the need for hospitalization [8,11,65].

Exercise self-efficacy

Self-efficacy is defined as the patient's confidence in the ability to perform a specific action in a specific situation [66]. It is thought that being able to reach a desired goal is less about having the right skills and more about the person's beliefs about what can be done with these skills in challenging situations. Self-efficacy beliefs can be general, disease specific, or tied to a specific action. Exercise self-efficacy is the specific self-efficacy referring to the confidence a person has in being physically active. A high exercise self-efficacy is needed for optimal exercise behavior [66,67]. This has been studied in both COPD and CHF patients [68,69].

According to the self-efficacy theory, four factors influence an individual's level of self-efficacy: past successful or unsuccessful performance, verbal persuasion by a trusted person, emotions caused by physiological re-

sponse to the exercise, and "modeling" [70,71]. Modeling means that a patient's self-efficacy can increase by seeing or hearing someone in the same situation solving problems and succeeding. It is a powerful tool in self-management education and its positive effect can be achieved in group-oriented programs.

Relationship between patient outcomes

Management of chronic diseases aims to improve or maintain the patient's quality of life, and to do that it is important to understand what patient outcomes are associated with health status and how they interact. To investigate the relationship between different patient outcomes, a conceptual model based on the revised Wilson and Cleary model was used [72]. This model hypothesizes a potential pathway from chronic disease to patient-reported outcomes such as general health perception and overall quality of life. The model proposes a pathway of linkages between five domains extending from biological function, symptoms, functional status, and general health perceptions to overall quality of life. For every component, this pathway is influenced by characteristics of the individual and the environment. The model uses arrows to represent the dominant causal relationships. However, reciprocal relationships between the variables are recognized to exist. Also, the existence of both direct and indirect relationships between the domains has been studied [73].

The conceptual model used in this thesis does not include biological function and overall quality of life. This model describes the relationship of five symptoms frequently present in both COPD and CHF with physical capacity and health status. For every component, this pathway is related to exercise self-efficacy as an important characteristic of the patient (Figure 3).

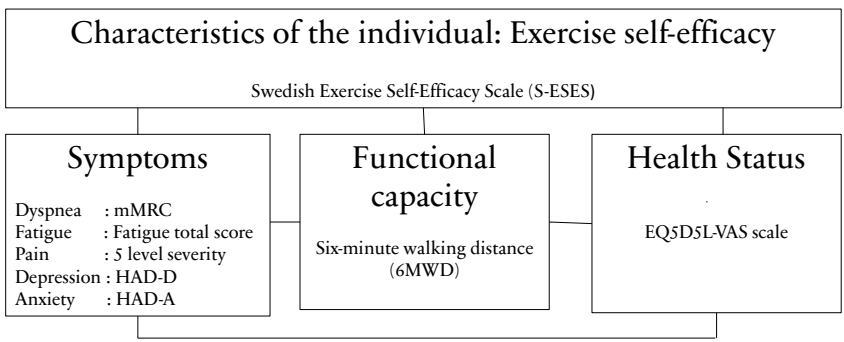

Figure 3. Conceptual model of the relationship between variables in patients with COPD and CHF.

Rationale for this thesis

Management of the growing group of patients with COPD and chronic heart disease is complex and largely occurs in primary health care. The focus in the management of COPD and chronic heart disease is to prevent periods of deterioration and disease progress, to maintain the best possible quality of life for the patients, and to help the patients manage their diseases and limitations in daily life. As the core competencies of general practice permit this task to be successfully fulfilled, more knowledge of the specific circumstances of primary health care is needed.

In the management of CHF, adherence to guidelines for diagnosis and treatment has been proven to reduce mortality, morbidity, and hospitalization and improve the patient's quality of life [11,74]. In spite of this, several studies have shown that not all patients with a heart failure diagnosis have been examined with ultrasound cardiography and that recommended medication is not always prescribed, especially not in target doses [75,76]. To improve guideline adherence by GPs, it is necessary to know to what extent the guidelines are currently followed and where GPs deviate from these guidelines.

A patient-centered approach requires a shift of focus from diagnosis to patient outcomes. Patients with COPD and CHF share symptomatology, the diseases often coexist, and the exercise recommendations are similar [77]. Therefore, it seems logical to assume a beneficial modeling effect when patients with CHF and COPD are enrolled in the same self-management education group with a focus on increasing exercise self-efficacy. However, little is known of whether the level of exercise self-efficacy in these two patient groups is similar. Exercise self-efficacy has been studied in both COPD and CHF patients, but levels are hard to compare because these studies have often focused on general self-efficacy or used disease-specific instruments. It also is important to know whether the relationship between exercise self-efficacy and other patient outcomes, such as symptoms, functional capacity, and health status, as assumed by the conceptual model, are comparable for both COPD and CHF patients.

The general population is aging, and this means that patients with COPD will need follow-up in primary health care for many years. Comorbid heart disease is common in patients with COPD. It has also been reported that health status and symptoms worsen over time in patients with COPD [78-80]. To give optimal care to these patients, it important to know the impact of comorbidity on symptoms, health status, hospitaliza-

tion, and mortality over a longer period in the unselected primary care population. More knowledge is needed in this area since not many studies have examined a real-life population over a longer period, including the specific causes of death and hospitalization.

Overall aim of the thesis

This thesis will explore different aspects of the management of patients with COPD and chronic heart disease in primary health care.

The specific aims are:

I. To describe adherence to international guidelines for chronic heart failure (CHF) management for diagnostic testing, pharmacological treatment, and self-care behavior in primary health care.

II. To compare the level of exercise self-efficacy, symptoms, functional capacity, and health status and to investigate the association between these outcomes in patients with COPD and CHF. Additionally, to investigate how diagnosis, symptoms, and patient characteristics are associated with exercise self-efficacy in these patient groups.

III. To examine the changing influence over time of comorbid heart disease on symptoms of dyspnea and health status in patients with COPD.

IV. To examine the association of comorbid heart disease with all-cause and cause-specific hospitalization and mortality in a cohort of patients with COPD over a period of nearly 15 years.

Materials and methods

This thesis contains data gathered from three study populations. The methods used are summarized in Table 1.

Patients and data collection

Study I

All patients from three primary health-care centers (PHCCs) in Värmland with a doctor's diagnosis of heart failure in their medical records between May 2010 and November 2013 were selected. Patients living in nursing homes were excluded from the study. Questionnaires were sent out to 246 patients, and 155 (63%) patients returned them and gave their consent to a record review. The questionnaire contained questions about the patient's social situation, knowledge of their heart failure diagnosis, and self-care behavior. The records were reviewed for diagnostic tests and chronic comorbidity (2007–2015), health care contacts (May 2012–November 2013), and medication (2015). To evaluate adherence to guidelines, the ESC guidelines published in 2012 were used [26].

Study II: Symptoms and function study (SAFS)

This study used the baseline data collected from 150 patients enrolled in the Symptoms and Function Study (SAFS), an intervention study testing a joint self-management group intervention for patients with COPD and CHF recruited in primary health care with the goal of increasing the patients' self-efficacy [16]. Patients with spirometry-verified COPD or an ICD-10 code for heart failure (I50) were consecutively selected from nine PHCCs in Sweden. To be included, the patients should have at least one symptom of dyspnea, fatigue, pain, or sleeping disorder. Moreover, the patients' disease should be in a stable state. The patients were excluded if they had had an exacerbation of their COPD or a heart infarction in the last three months. Additional exclusion criteria were patients living in nursing homes, with mental impairment, and insufficient knowledge of the Swedish language. Patients who stated in the questionnaire that they had both diseases or declared having the other diagnosis than they were selected for were considered to have a patient-reported double diagnosis. In this way, we had a group of 150 patients, 60 with a spirometry-verified diagnosis of COPD, 60 with a doctor's diagnosis of CHF, and 30 with a patient-reported double diagnosis. The questionnaires gathered information

about age, sex, social status, level of physical activity, and smoking habits; they also contained instruments for measuring symptoms, health status, and self-efficacy.

Table 1. M*aterial and methods for the four studies included in this thesis.*

	Study I	Study II	Study III	Study IV
Method	Cross-sectional Questionnaires Medical record review	Cross-sectional Questionnaires	Cohort Questionnaires Medical record review	Cohort Questionnaires Medical record review Register data
Main outcomes	Guideline adherence Self-care behavior (EHFScBS-9)	Exercise self-efficacy (S-ESES), Health status (EQ5D-VAS), 6-minute walking distance, mMRC fatigue score, HAD, pain	Health status (CCQ, CAT) Dyspnea (mMRC)	Hospitalization Mortality
Selection criteria	Diagnosis of heart failure (I 50)	Diagnosis of heart failure (I 50) or COPD (J44)	Diagnosis of COPD Age 34–75	Diagnosis of COPD Age 34–75
Patient selection	3 PHCCs in Värmland	5 PHCCs in Healthcare region Mid Sweden	56 PHCCs and 14 hospitals in Healthcare region Mid Sweden	56 PHCCs and 14 hospitals in Healthcare region Mid Sweden
Study period	Q 2015 MRR 2007–2015	Q 2013	Q 2005 and 2012 MRR 2000–2012	Q 2005 MRR 2000–2003 RD 2005–2019
Participants	155	150	346–468	1071
Statistics	Student's *t*-test Chi square Logistic regression	Student's *t*-test Chi square Mann-Whitney U-test Spearman correlations Linear regression	Student's *t*-test Chi square Linear and logistic regression	Student's *t*-test Chi square Cox and linear regression
Ethical approval, Uppsala	Dnr 2014/279	Dnr 2012/189/1	Dnr 2004:M–445 Dnr 2011/318	Dnr 2004:M–445 Dnr 2010/090, Dnr 2020–00270

Abbreviations: MRR = medical record review, Q = questionnaire, RD = register data, PHCC = primary health-care center, Dnr=Diarienumber

Studies III and IV: PRAXIS

The PRAXIS study is based on data from 14 hospitals and 56 PHCCs in Healthcare region Mid Sweden. In total, 1548 patients were randomly selected from lists of patients aged 34–75 years with an ICD-10 diagnosis code J44 for COPD recorded in their medical records during the 2000–2003 period. A questionnaire was sent to these patients in 2005; 1071 (69%) returned the questionnaire and agreed to a review of their medical records. In 2012, all patients who were still alive received a questionnaire similar to that in 2005. A total of 561 patients returned both the baseline and follow-up questionnaires. The Swedish Board of Health and Welfare provided hospitalization and mortality data on the participating patients for the 2005–2019 period. These data included information about the date and underlying cause of death, date(s) and main cause(s) of hospitalization. For the patient and mortality register, the ICD codes I 00–I 99 were used to indicate an outcome of cardiovascular disease and death [81]. Cardiovascular disease is a general term for diseases affecting the heart and blood vessels. This group therefore includes, besides CHF and chronic ischemic heart disease, other acute and chronic afflictions of the heart, such as valvular disease and arrhythmias, as well as peripheral and cerebrovascular disease. The ICD codes J 00–J 99 were used to indicate respiratory disease and death.

The record review provided information on a doctor's diagnosis of heart disease, hypertension, depression, and diabetes as well as data on lung function. For study III, the study population was divided into three groups: COPD patients without a diagnosis of heart disease (no HD), those diagnosed with heart disease during the study period (new HD), and those who had a heart disease diagnosis at the start of the study (HD). For study IV, the study population was divided into two groups: patients with and without a comorbid heart disease at baseline.

The questionnaires gathered information on age, sex, smoking status, education level, exacerbations in the previous six months, height, weight, symptoms, and health status.

Measurements

Self-care behavior (study I)

Self-care behavior was measured using the European Heart Failure Self-care Behaviour Scale (EHFScBS). The scale was originally a 12-item questionnaire developed in a Swedish, Dutch, and British population and later

reduced to a nine-item version and tested for good validity and reliability [82,83]. The items are scored on a five-point scale ranging between 1: "I completely agree" and 5: "I completely disagree." The possible range of scores for the total EHFScBS-9 is between 9 and 45, with a lower score indicating better self-care behavior. The scale contains questions about daily weighing, fluid and salt restriction, regular exercise, and consulting behavior when symptoms increase.

Exercise self-efficacy (study II)

Exercise self-efficacy was measured using the Swedish validated version of the SCI Exercise Self-Efficacy Scale (S-ESES) [84]. This scale consists of 10 statements about confidence in performing exercise in different situations, for example, when feeling tired or without the support of family and friends. The statements are scored on a four-point Likert scale where 1 = "not at all true," 2 = "rarely true," 3 = "moderately true," and 4 = "always true." The total score ranges from 10 to 40, with 40 indicating the highest level of exercise self-efficacy.

Symptoms (studies II–IV)

Dyspnea (studies II– IV)

The modified Medical Research Council Dyspnea score (mMRC) measured the level of dyspnea. The mMRC has five points ranging from 0 = "I only get breathless with strenuous exercise" to 4 = "Too breathless to leave the house or breathless when dressing or undressing" [85]. A score of 0 or 1 corresponds to a low level of dyspnea , and scores of 2 and higher denote increasing limitations of activity due to dyspnea during daily life. The scale is validated and frequently used in clinical and research settings [85].

Fatigue (study II)

Fatigue was assessed with three questions and calculated into a total score for frequency, duration, and severity (range 0–9) [86]. The frequency of fatigue over the past month was scored as 0 = not a problem, 1 = 1–7 days a month, 2 = 8–14 days a month, 3 = 15–21 days a month, and 4 = 22–30 days a month. The duration of fatigue was scored as 0 = no experience, 1 = less than 6 hours a day, 2 = 6–12 hours a day, and 3 = more than 12 hours a day. The severity of fatigue was scored as 0 = not a problem, 1 = one of my less severe problems, and 2 = one of my worst symptoms.

Depressive and anxiety symptoms (study II)

Symptoms of depression and anxiety were assessed by the Swedish version of the Hospital Anxiety and Depression scale (HAD). It consists of seven items in two subscales (score range, 0–21) and measures the degree of anxiety (HAD-A) and depression (HAD-D). A higher score indicates a higher level of depressive or anxiety symptoms. In clinical practice, a HAD score over 8 can be indicative of the presence of the respective mood disorder [87].

Pain (study II)

Severity of pain was assessed using the patients' answer to the question about their current level of pain or discomfort from the questionnaire developed by the EuroQol Group (EQ5D5L). The question was answered on a five-point Likert scale ranging from 0 = "I have no pain or discomfort" to 4 = "I have extreme pain or discomfort" [88].

Functional capacity (study II)

The functional capacity of the patients was assessed using the six-minute walking distance test (6MWD), in which the patient had to walk as far as possible for six minutes after receiving standardized instructions [61].

Health status (studies II and III)

To assess general health status, the visual analogue scale from the EuroQol Group (EQ5D5L-VAS) was used. The patients were asked to rate their perceived health that day on a vertical VAS scale of 0–100, with 0 being the worst and 100 the best imaginable health [88].

To measure disease-specific health status, the Clinical COPD Questionnaire (CCQ) and the COPD assessment test (CAT) were used. The CCQ included ten items about the patient's health the previous week, distributed over three domains: symptoms, mental state, and functional state [89]. The symptoms domain contained questions on dyspnea, cough, and phlegm; the mental state domain assessed feelings of depression and concerns about breathing or getting worse; and the functional state domain assessed limitations in different activities of daily life due to lung disease. Answers were given on a seven-point scale ranging from 0 to 6. In this way, a total mean score and separate mean scores for each domain could be calculated, with a higher score indicating lower health status. The CAT included eight items about the patient's experience of cough, mucus production, chest tightness, dyspnea on exercise, limitation of activities at

home, sense of confidence about leaving the home, sleep, and energy level [90]. The patient scored the symptoms on a six-point scale ranging from 0 to 5. The sum score can range from 0 to 40, with a higher score indicating lower health status. The CCQ and CAT correlate well with each other and can be used as equivalents for measuring health status [90-92].

Statistical analysis

Categorical data were expressed using frequencies and percentages. Continuous data were presented as means and standard deviations or, when non-normally distributed, as medians with interquartile ranges. Differences between groups were analyzed using the Chi-squared test, Mann–Whitney U-test, or Student's *t*-test for independent groups. The level of statistical significance was set at $p < 0.05$. All analyses were performed using IBM SPSS versions 21–28.

In study I, binary logistic regression analysis was used to investigate the effect of EF, age, sex, and health-care contacts on the prescription of medication and the effect of EF, age, and sex on health-care contacts.

In study II, Spearman correlation coefficients were used to analyze the correlation between the different variables within the conceptual model (Figure 3). The Bonferroni–Holm method was used to correct for the use of multiple variables [93]. Regarding values of the correlation coefficient, 0–0.19 was regarded as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong, and 0.8–1 as very strong correlation [94]. Linear regression analyses, unadjusted and adjusted for diagnosis group (i.e., COPD, CHF, and double diagnosis), sex, and age, were used to analyze what variables were associated with the level of exercise self-efficacy.

In study III, logistic regression with mMRC ≥ 2 and linear regression with CCQ and CAT scores in 2012 as dependent variables were performed unadjusted, adjusted for potential confounders, and additionally adjusted for baseline mMRC and CCQ scores, respectively. Beside sex, only associated variables in the univariate regression were included in the adjusted regression analysis. For the linear regression with CCQ and CAT, these variables were sex, age, educational level, exacerbations in the previous six months in 2005, and heart disease. For the analysis with mMRC, the potential confounders were sex, age, exacerbations in the previous six months in 2005, and heart disease.

In study IV, Kaplan–Meier (KM) curves and Cox regressions assessed survival [95]. Study entry was defined as the date when the patient's questionnaire was sent out. For hospitalization analysis, follow-up time was

defined as the time from study entry until the first hospitalization, death, or the end of the study on 31 December 2019. Follow-up time for mortality analysis was defined as the time from study entrance until death or the end of the study on 31 December 2019. The KM curve indicated that the proportional hazards assumption was justified for mortality data. Because of convergence of the lines of the KM curve for first hospitalization, truncation after eight years was used as a sensitivity analysis [96]; this truncated analysis gave comparable results. Cox regression was used to assess univariate associations with hospitalization and mortality for baseline data on heart disease, age, sex, smoking status, education level, a diagnosis of diabetes, depression, hypertension, BMI group, exacerbations, and mMRC. All variables significant at $p < 0.05$ were included in a multivariate analysis. Cause-specific hospitalization and mortality associations with comorbid heart disease were assessed by Cox regression analysis using the same variables as in the all-cause mortality and hospitalization analysis.

In both studies III and IV, all analyses were repeated in the subgroup with available spirometry data. Stratification and multiplicative interaction analyses investigated the potential effect of modification by sex and age for all regression analyses.

Ethical approval

All studies in this thesis were performed in accordance with the Declaration of Helsinki and were approved by the Regional Ethical Review Board of Uppsala. Since all studies were descriptive studies, there was no risk of any adverse effect of an intervention on the participating patients. For this reason, the Regional Ethical Review Board of Uppsala regarded approval of the PRAXIS study as unnecessary in 2005 (Dnr 2004:M–445). After 2005, the regulations about when ethical approval is obligatory were changed. For this reason, new ethical approval was obtained for sending out new questionnaires in 2012 (Dnr 2011/318) and for the use of register data (Dnr 2010/090, Dnr 2020–00270). Written consent was obtained from all participants (studies I–IV) and the patients were informed that their participation was voluntary and could be withdrawn any time.

Results

Study I

Patient characteristics

Patients in study I had a mean age of 79 (SD 9) years. The women (n = 66) were significantly older than the men (n = 89) with a mean age of 82 (SD 10) versus 78 (SD 8) years. The men were significantly more often diagnosed with ischemic heart disease and atrial fibrillation than were the women. To the question of whether they were aware of having a heart failure diagnosis, 33% of the patients answered that they did not know.

Between May 2012 and November 2013, 40% of the patients had had contact with a hospital outpatient clinic or had been hospitalized for their CHF. In total, 16% of the patients had had contact with a hospital heart failure clinic between 2011 and 2015. An EF ≤ 40% was the only statistically significant clinical factor for referral to this type of outpatient clinic.

Diagnostic procedures

All patients had undergone an electrocardiogram (ECG) and the laboratory values of the natriuretic peptides were known in 87% of the patients. Transthoracic echocardiography (TTE) was performed in 82% of the patients. Stratification for sex and age showed no statistically significant differences between these groups in these parameters. Of the patients with a hospital contact, 97% had been examined with TTE. The mean left ventricle EF was 46% (SD 15); for men, this was 42% (SD 15) and for women 52% (SD 12), which were significantly different values.

Pharmacological treatment

The percentages of patients prescribed the different types of pharmacological treatment are given for patients with EF ≤40% and >40% in Figure 4. Women were prescribed significantly less of the RAS inhibitors, in terms of target dose, than were men, even after correction for age, EF, and kidney function. Patients with a lower EF were significantly more often prescribed BB and the combination of BB and RAS inhibitors. BB and MRA were prescribed more frequently to those who had received hospital care, independently of EF. Patients who had been in contact with a hospital heart failure clinic were more often prescribed BB at the target dose.

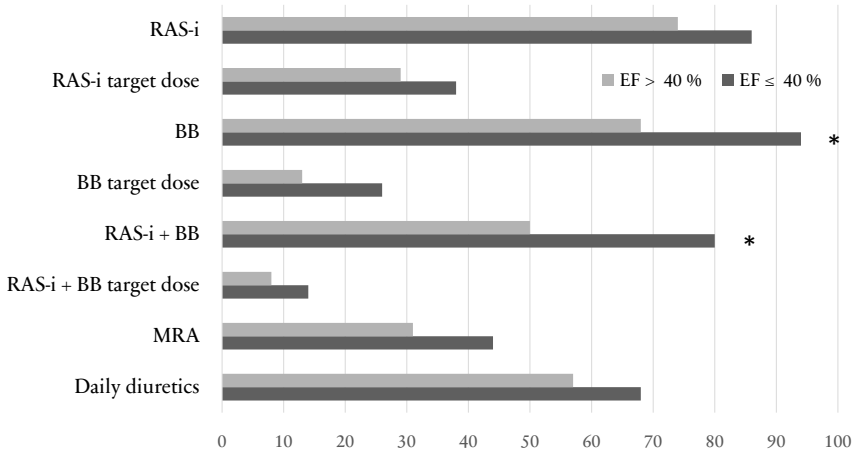

*Figure 4. Percentage of patients with HFrEF (EF ≤40%, dark bar) prescribed recommended medication. These recommendations do not apply to patients with EF >40% (light bar), but data for this group is shown for comparative reasons. * Statistically significant difference (p < 0.05) between the two groups.*

Self-care behavior

The mean score on the EHFScBS-9 was 29 (SD 6) on a scale ranging from 9 (best self-care behavior) to 45 (worst self-care behavior). There was no statistically significant difference in score between patients who knew that they had CHF and those who did not. The patients who had been in contact with a hospital heart failure clinic had a statistically significantly better mean score of 24 (SD 7), compared with 30 (SD 6) for those who had not. Almost all patients agreed totally with the statement that they always took the prescribed medication. More than half of the patients had a score of five ("I completely disagree") for the statements on "daily weighing" and "contacting health care when gaining more than 2 kg in seven days."

Study II

Patient characteristics

Patients with COPD (n = 60) were on average younger than patients with CHF (n = 60), with a mean age of 69 (SD 8) compared with 78 (SD 8) years.

The group with a double diagnosis (n = 30) had a mean age of 72 (SD 6) years. There were fewer men (48%) in the COPD group than in the CHF group (77%).

Comparison of patient outcomes

No statistically significant difference was found in the patient-reported exercise self-efficacy, health status, dyspnea, fatigue, pain, and symptoms of depression and anxiety. The only patient outcome that was significantly different between the groups was functional capacity measured by the six-minute walking distance, although this difference was not statistically significant when adjusted for age. Stratification for sex showed no difference between men and women.

Relationship between patient outcomes

Within the conceptual model (Figure 3) of patients with COPD, statistically significant weak to moderate correlations were found for exercise self-efficacy with health status and symptoms of depression and anxiety and, furthermore, for health status with functional capacity, dyspnea, pain, and depressive symptoms. In patients with CHF, statistically significant weak to moderate correlations were found for health status with symptoms of pain, depression, and anxiety. In the analysis of the whole group (n = 150), significant but mainly weak correlations were found between most of the variables within the model, except for functional capacity with fatigue and symptoms of anxiety.

Factors associated with level of exercise self-efficacy

Linear regression analysis showed that the level of exercise self-efficacy was negatively associated with increasing dyspnea, fatigue, pain, and depressive and anxiety symptoms, even after adjustment for sex, age, and diagnosis. No association was found for a diagnosis of COPD, CHF, or both diseases. In the univariate regression analysis, higher age was significantly associated with lower exercise self-efficacy, but this association was no longer significant when adjusted for diagnosis and sex.

Studies III and IV

Patient characteristics

In both studies III and IV, COPD patients with comorbid heart disease were significantly older and more often male. The 495 patients with

COPD in study III were divided into three groups: COPD patients with comorbid heart disease at baseline (n = 103); COPD patients who were diagnosed with heart disease during the study period (n = 58); and COPD patients without comorbid heart disease (n = 334). In study IV, 262 (25%) of the 1071 patients had heart disease at baseline.

Dyspnea

In 2005, mMRC scores were significantly higher in the group with heart disease at baseline and in those who later, during the study, developed heart disease. A new assessment of the mMRC in 2012 showed that there was an increase in dyspnea during the study period in all groups (Figure 5). In the groups with and without heart disease, this increase was found to be statistically significant. The logistic regression analysis for mMRC showed that comorbid heart disease throughout the study period was an independently statistically significant factor associated with a higher mMRC score at follow-up; after correction for baseline mMRC, however, no significant associations were found.

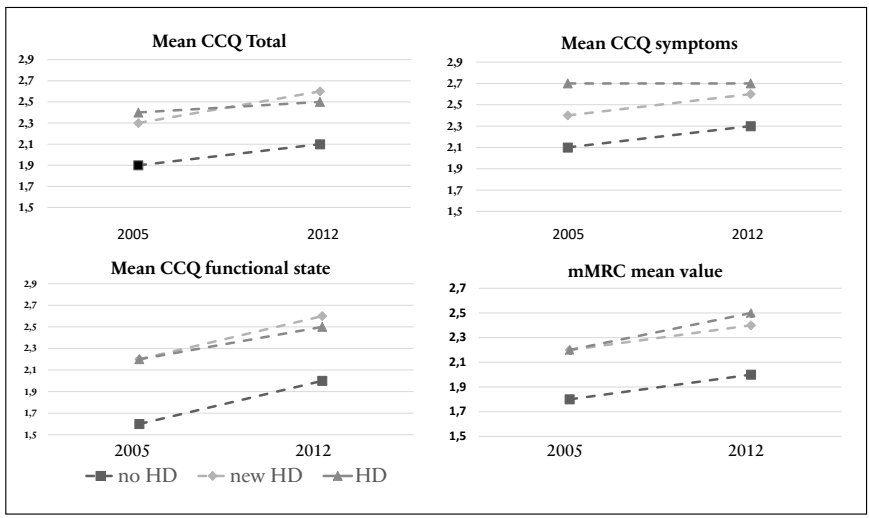

Figure 5. Mean CCQ and mMRC scores in 2005 and 2012 in patients with COPD without heart disease (no HD), with heart disease diagnosed during the study period (new HD), and with heart disease at baseline (HD).

Table 2. *Regression analyses with CCQ, CAT, and mMRC ≥2 in 2012 as dependent variables.*

	Regression coefficient (95% CI)	*p*-value	**Regression coefficient (95% CI), adjusted for confounders**	*p*-value	**Regression coefficient (95% CI), adjusted for confounders and baseline CCQ**	*p*-value
No HD	Ref	Ref	Ref	Ref	Ref	Ref
Linear regression CCQ total						
New HD	0.47 (0.04-0.90)	0.03	0.46(0.05–0.88)	0.03	0.22(-0.11-0.56)	0.19
HD	0.43(0.05–0.82)	0.03	0.33(-0.05-0.71)	0.09	0.07(-0.24-0.37)	0.67
Linear regression CCQ symptoms						
New HD	0.37(–0.06–.80)	0.09	0.35 (–0.07–0.76)	0.01	0.21(–0.13–.55)	0.23
HD	0.39(0.01–0.76)	0.04	0.22 (–0.16–0.60)	0.45	–0.01(-0.33-.30)	0.94
Linear regression CCQ functional state						
New HD	0.68 (0.17–1.20)	0.01	0.67 (0.18–1.16)	0.01	0.31(-0.11-0.72)	0.15
HD	0.58 (0.13–1.03)	0.01	0.49 (0.04–0.92)	0.03	0.19(-0.19-0.58)	0.32
Linear regression CAT						
New HD	3.13 (0.30–6.00)	0.03	3.15 (0.04–5.91)	0.03	1.59(-0.68-3.85)	0.17
HD	3.93 (1.44–6.43)	0.002	3.40 (0.89–5.92)	0.01	1.68(-0.40-3.76)	0.11
Logistic regression mMRC ≥2						
	OR (95% CI)	*p*-value	**OR (95% CI), Adjusted for confounders**	*p*-value	**OR (95% CI) adjusted for confounders and baseline mMRC**	*p*-value
New HD	1.45 (0.80-0.61)	0.22	1.37 (0.74–2.53)	0.32	0.99 (0.49-0.99)	0.99
HD	1.74(1.08–2.81)	0.02	1.71 (1.03–2.86)	0.04	1.44(0.81–2.56)	0.21

Health status

At baseline, the CCQ total score and the scores in the symptom and functional state domains were significantly higher in the group with heart disease at baseline than in the group without this comorbidity (Figure 5). The group with newly diagnosed heart disease had a significantly higher score in the functional state domain. There was no significant difference for the score in the mental state domain, and the score in this domain did not

worsen between 2005 and 2012. Between 2005 and 2012, there was a statistically significant worsening of the mean CCQ, mean CCQ symptoms, and mean CCQ functional state in the group of patients without heart disease and in the group with incident heart disease. Health status also worsened in the patients with comorbid heart disease at baseline, but this worsening was not found to be statistically significant.

Adjusted linear regression analysis showed that comorbid heart disease at baseline was significantly associated with a worse CCQ functional state and higher CAT score in 2012. The table printed in the journal article contains some errors [97]; the corrected table is presented as Table 2. Incident comorbid heart disease was significantly associated with worse CCQ total, worse CCQ functional state, and higher CAT scores. The CCQ mental state domain had no significant associations with heart disease. After adjustment for baseline CCQ, no statistically significant associations of heart disease with worse health status as assessed by CAT or CCQ, total and all domains, over time were found.

Interaction, stratification, and subgroup analyses for study III

The interaction analyses for both dyspnea and health status showed no statistically significant effect modification by sex or age for any of the associations (data not shown). Adjusted regression analysis in the subgroup with available spirometry data (n = 216) showed a statistically significant association of comorbid heart disease with CAT score, but not with mMRC ≥ 2, CCQ total or any of its domains (data not shown).

Hospitalization

From 2005 through 2020, 721 (89%) COPD patients without heart disease and 247 (93%) with comorbid heart disease had been hospitalized at least once. Of the patients without heart disease at baseline, 403 (53%) had been hospitalized for a respiratory disease during the study period compared with 153 (58%) with comorbid heart disease ($p = 0.02$). For cardiovascular disease, these numbers were 285 (35%) compared with 133 (51%), respectively ($p < 0.001$), and for other reasons, 542 (67%) compared with 207 (79%) hospitalized patients ($p < 0.001$).

Adjusted Cox regression analysis showed that comorbid heart disease was significantly associated with higher risks of all-cause, cardiovascular, and other causes of hospitalization, but not with a higher risk of respiratory hospitalization (Figure 6).

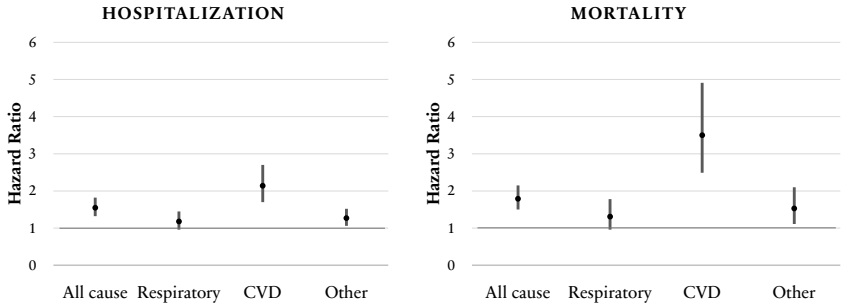

Figure 6. Hazard ratio for comorbid heart disease for hospitalization and mortality in patients with COPD, at 15-year follow-up.

Mortality

By the end of 2019, 438 (54%) of the patients without comorbid heart disease and 222 (85%) of the patients with comorbid heart disease had died. Of the patients without heart disease at baseline, 192 (24%) died of a respiratory disease compared with 71 (27%) with comorbid heart disease ($p = 0.003$). For a cardiovascular cause of death, these numbers were 83 (10%) compared with 85 (23%), respectively ($p < 0.001$), and for other causes of death, 163 (20%) compared with 66 (25%) ($p = 0.06$, not significant).

Cox regression analysis, adjusted for confounders, showed that comorbid heart disease was significantly associated with higher risks of all-cause, cardiovascular, and other causes of mortality, but not with a higher risk of respiratory mortality (Figure 6).

Stratification, interaction, and subgroup analyses for study IV

Stratification for sex revealed differences between men and women in the associations of comorbid heart disease with both hospitalization and mortality. The associations of comorbid heart disease with respiratory and other causes of hospitalization and mortality were found to be statistically significant in women, but not in men. Furthermore, the hazard ratio was higher for cardiovascular hospitalization and mortality. However, these differences were not significant at interaction analysis.

The interaction analyses showed no statistically significant effect modification by age for any of the associations. In the subgroup with available spirometry data, similar associations were found, except that there was no significant association between heart disease and other causes of hospitalization and death.

Discussion

Main findings

Adherence to the guidelines for diagnostic testing, pharmacological treatment, and patient self-care behavior in primary health care was found to be suboptimal. One out of five patients with a CHF diagnosis had not been examined with ultrasound cardiography. Recommended medications were given to most of the patients, but only a few achieved target doses. One out of three patients was unaware of having a CHF diagnosis and self-care behavior was suboptimal. Attending a hospital heart failure clinic improved adherence to guideline recommendations.

Patients with COPD and CHF have similar levels of exercise self-efficacy, health status, functional capacity and dyspnea, fatigue, pain, and depressive and anxiety symptoms. Higher exercise self-efficacy was associated with lower level of symptoms, but not with the diagnosed disease.

Comorbid heart disease in patients with COPD was associated with a lower health status and higher level of dyspnea, but did not accelerate the worsening over time. Comorbid heart disease was also associated with an increased risk of all-cause hospitalization and mortality, mainly due to an increase in hospitalization and death of cardiovascular and other causes, but not of respiratory disease.

Methodological considerations and limitations

Generalizability

The patients included in study I came from an unselected population, but from only three PHCCs within a restricted area. This could be a limitation for generalizability to other regions or countries. However, the prevalence of CHF and the patient characteristics found in this study were as expected in primary health care [14]. Also, the results of study I were in line with the results of similar studies of larger populations and in other countries with comparable health-care systems [98,99]. Study I had a response rate of 63%. Comparison of responders and non-responders showed that women, especially those over 85 years old, were not fully represented in this study. Generalization of our findings to the elderly CHF population must therefore be done carefully.

For study II, patients in the stable phase of their disease were selected. The patients who were included agreed to participate in a group interven-

tion, and that might have caused a selection bias: it might have been that patients with high motivation and less severe disease were overrepresented. However, regarding age and sex differences, the frequency and level of symptoms in both groups are comparable to those found earlier in Swedish primary care in an unselected population [58].

The patients in studies III and IV were randomly selected, at multiple primary and secondary care centers, from an unselected population of patients with COPD in Healthcare region Mid Sweden, ensuring a high level of generalizability of the results to clinical practice. However, to enable a long follow-up time, an upper age limit of 75 years was set as a selection criterion. This resulted in a lower prevalence of comorbid heart disease at baseline than in previous studies in Sweden [31,100]. Generalization of the findings to the elderly COPD population must thus be done carefully. The patients selected from hospital clinics were not excluded, since they are also managed in primary health care, if not for their COPD, then for comorbidity and other non-chronic afflictions. The response rate for the PRAXIS cohort at baseline was 69% and attrition analysis of the responders and non-responders showed no clinical difference between the groups.

Patients in nursing homes were excluded from studies I and II. It is also to be expected that few patients in the PRAXIS studies were living in nursing homes at baseline because of the 75 years limit at inclusion. The prevalence of both COPD and CHF is high in the elderly and multimorbid population of nursing homes. Generalization of the results of studies I-IV to this special group patients must be done cautiously. Further research, also with a qualitative approach, is needed.

Questionnaires and medical records review

Studies I, III, and IV combine information from both questionnaires and medical records, giving the opportunity to study both the patient and health care perspectives.

All diagnoses, except for the COPD patients in study II, were based on a doctor's diagnosis in the medical records and were not validated. This might be a limitation, since misdiagnosis of both COPD and CHF is not unusual [101,102], but it represents the clinical reality in everyday praxis.

As a result of selecting patients based on a doctor's diagnosis without verification, there was no spirometry data for half of the patients in the PRAXIS cohort [103]. The possible confounding factor of COPD severity grading could therefore not be included in the main analyses of studies III

and IV. Subgroup analysis was conducted for the group with spirometry data, producing results similar to those found in the main analyses in both studies III and IV.

Conceptual model

To clarify the research question and outcomes for study II, a conceptual model was used. A conceptual model provides a visual schema that represents a research question, and often an existing model is used as a basis [104]. It is a much-used technique to use an existing model already tested in a population and to adapt it to one's own research question. Models have to be kept simple, and not all possible factors and pathways found in the complex reality can be considered [104].

Few statistically significant and mainly weak correlations were found in the conceptual model for study II. A problem with the model testing was the relatively small number of patients in the separate diagnosis groups, which probably caused that few significant correlation coefficients were found in the model for COPD and CHF separately. When a sample size is too small, a study can fail to find a difference that is actually there—a type II error [105]. The fact that more and stronger significant correlation coefficients were found in the group as a whole supports this assumption and indicates that this conceptual model is applicable to both COPD and CHF patients.

The fact that we found fewer and weaker associations in the model for patients with CHF might, on the other hand, indicate that other variables, such as comorbidity and social and environmental factors, not included in our model play a larger role in patients with CHF [106,107]. Few other studies have compared patients with COPD and CHF, but similarities and differences between the two disease groups have previously been found in a study exploring the relationship between dyspnea, functional status, and health status in patients with COPD and CHF [108].

Register data

The availability of data from the National Patient Register and Cause of death Register that could be matched to the patients in study IV made it possible to get detailed information on both all-cause and cause-specific hospitalization and mortality. These registers are compulsory and give a nearly complete account of all hospitalizations and deaths in Sweden. A limitation of these registers is that the diagnoses are not validated and can be inaccurate. Also, only the main cause of hospitalization and death is

considered, which does not always reflect the complexity of clinical reality. The absence of an association between comorbid heart disease and hospitalization and mortality due to respiratory disease in our study might be explained by this uncertain validity of diagnosis coding. COPD-related mortality and morbidity might be underestimated because it was difficult to attribute death and hospitalization to a single cause in the clinical setting. Cardiovascular disease might be prioritized when choosing the main diagnosis or cause of death. Underreporting of COPD as an underlying cause of death is a known problem especially in patients with mild COPD [109-113].

Discussion of the main findings

Guideline adherence in management of chronic heart failure (study I)

Transthoracic echocardiography

In study I, the number of patients in primary care assessed using transthoracic echocardiography is still inadequate, even though there has been a clear improvement since the early 2000s [75,114]. Assessment of cardiac function is essential in the management of CHF, since the evidence for treatment options differs between different heart failure groups. The recently launched standardized care program from the national system for knowledge-driven management in Swedish health care will hopefully support the GP in recognizing and referring all patients with suspected heart failure for echocardiography, resulting in no heart failure diagnosis being made without differentiating between HFrEF, HFmrEF, and HFpEF.

Pharmacological treatment

Only few patients with EF ≤40% reached target doses of the recommended medications. Also, besides beta blocker prescriptions, there was no significant difference in pharmacological treatment between the two EF groups in study I. This might be because cardiovascular comorbidity is treated with the same medication groups as recommended for HFrEF, but might also be because of the prescriber's unawareness of the difference in recommendations for HFrEF and HFpEF. The underuse of certain drugs and missed target doses in primary health care have previously been studied and seem to be caused by side effects, fear of side effects, adaptation to other comorbidity, lack of knowledge of the guidelines, and uncertainty of diagnosis [99,115].

Guidelines are recommendations and not the law, and can and must be deviated from if it is in the best interest of the patient. The evidence that guidelines are based on often comes from selected populations, so the guidelines are not always applicable to the often older and multimorbid patients with polypharmacy who are managed in primary health care [116]. Several disease-oriented guidelines might apply to the same patient, which complicates clinical decision making. To aid decision making in multimorbidity during primary care consultations, the Ariadne principles were developed [117]. It is important that the patient and GP share realistic treatment goals. The care management has to be based on a thorough interaction assessment; it has to be individualized and consider the patient's preferences.

This being said, the evidence for the benefit of the recommended pharmacological treatments is strong for patients with HFrEF, and these treatments have been proven to decrease mortality, decrease the need for hospitalization, and increase health status [11,74]. Fear of side effects, treatable side effects (e.g., high potassium levels), and lack of knowledge should not be reasons for deviating from the recommendations. A recently performed Swedish register study showed that patients with follow-up in primary health care had worse outcomes than did those who were managed in specialty care, even after adjustment for demographic and clinical variables [16]. A lot has happened in heart failure management in the last two decades. Study I was conducted at a time when the heart failure groups were not clearly defined and the existence of HFpEF was not generally known to general practitioners [118]. A qualitative study performed between 2017 and 2019 showed that HFpEF was not well understood by GPs, leading to diagnostic difficulty, management uncertainty and potential inequity in care offered [119]. It is therefore important that GPs have the time for education and for discussing complex patients with colleagues.

Self-care behavior

One out of three patients in study I reported not knowing that they had a heart failure diagnosis. The adherence to self-care recommendations was found to be low, particularly concerning daily weighing and consulting behavior when symptoms increase. The same results have been found in other European countries [120]. Good self-care behavior is important because it can reduce the need for professional help and hospitalization [64]. The fact that in study I there was no difference in self-care behavior

between the patients who were aware of their CHF diagnosis and those who were not suggests an insufficient system of patient education and monitoring. This is supported by the finding that the patients who had had contact with a hospital heart failure clinic had significantly better self-care behavior scores.

Heart failure clinics

Study I found statistically significantly better self-care behavior in and pharmacological treatment of patients who had contact with a hospital heart failure clinic. A beneficial effect on outcomes for patients with access to a heart failure clinic has been shown in both primary and secondary health care [121]. A recent meta-analysis on effectiveness of implementation interventions in improving physician adherence to CHF guideline recommendations concluded that working in multidisciplinary teams increased guideline uptake [122]. In primary health care in Sweden, structured care for COPD and diabetes is already solidly implemented with good results, and several regions have started nurse-led heart failure clinics in PHCCs [123]. Easy access to structured multidisciplinary care for heart failure patients in general practice is needed, as is further research on how this care and the therapy guidelines can be adapted to the specific needs of the often older and multimorbid patient population.

Patient outcomes in patients with COPD and CHF (study II)

Feasibility of combined COPD and CHF self-management groups

Patients with COPD and CHF had similar levels of health status, functional capacity, and symptoms as found in prior research [58,108]. Also, there was no difference in level of exercise self-efficacy between the groups, and exercise self-efficacy was not associated with the diagnosis of COPD or CHF. This creates conditions for a beneficial "modeling" effect when these patients are combined in a self-management group intended to increase exercise self-efficacy. The idea of a more symptom- and disability-focused rehabilitation instead of a strictly diagnosis-oriented approach has previously been discussed [124]. A hospital based pulmonary rehabilitation program has been shown to give good results in cardiac patients [125].

This study focused on the similarities between patients with COPD and CHF, but there are of course differences between these patient groups, for example, the use of diuretics in patients with CHF and sensitivity to cold

or damp air in patients with COPD. These problems need different strategies and make "modeling" more difficult. A pilot study for a combined breathlessness rehabilitation program for patients with COPD and CHF indicated clinical effectiveness and was received positively by both patients and health professionals [126]. Further research on the effectiveness of joint self-management groups and qualitative research on patient and caregiver experiences is needed for further evaluation of the feasibility of these groups in primary health care.

Exercise self-efficacy and symptoms

In the management of patients with COPD and CHF, dyspnea and fatigue are often considered, as these symptoms are directly linked to the pathophysiology of both diseases. However, pain, depression, and anxiety are not directly linked to the pathophysiology of the diseases but are nevertheless present in many patients with COPD and CHF, in whom they are often undertreated [127]. In study II, moderate to severe pain was found to be associated with reduced exercise self-efficacy. Pain has been shown to cause functional limitations, physical inactivity, and a lower health status in both COPD and CHF patients [106,128]. Also, anxiety and depression have been found to have a negative influence on patient self-efficacy [129,130]. On the other hand, it has been shown that an increased level of exercise will have a positive effect on the levels of pain and depressive symptoms [131]. The association between symptoms and exercise self-efficacy might be bidirectional or be mediated by other variables, such as actual physical exercise. Most patients in study II reported symptoms of depression and anxiety under a level that indicates a depression or anxiety disorder, but it seems that even symptoms of this low level are negatively associated with the patient's exercise self-efficacy. A recently published study showed that issues such as psychological wellbeing, stress, and fatigue are often underemphasized in self-management education [132]. Discussing these issues and supporting patients in finding strategies to address them would facilitate rehabilitation efforts.

Comorbid heart disease in COPD (studies III and IV)

Dyspnea and health status

Dyspnea and health status are both important patient-reported outcomes that are used to guide pharmacological treatment in patients with COPD [8,24]. Study III showed that comorbid heart disease negatively influenced

the patients' health status, as previously described in cross-sectional studies [133,134]. The finding that comorbid heart disease did not accelerate the worsening in health status and dyspnea over a seven-year period is consistent with findings of another study with a three-year follow-up [135]. In 2012, study III added data on CAT scores, which is important since CAT is now mainly used for the assessment of COPD patients in daily practice [8].

Comorbid heart disease especially seemed to worsen health status in the functional state domain, which is consistent with a study finding that self-reported heart disease markedly reduced the functional capacity measured by the six-minute walking distance [136]. Study III showed that this finding remains over time and that the reduced functional state can be detected using the CCQ questionnaire.

Hospitalization and mortality

The finding that comorbid heart disease is associated with increased long-term hospitalization and mortality risk in COPD patients is not unexpected, but this study adds novel data regarding long-term outcome, which is relevant to management in primary health care.

Comorbid heart disease did not increase the risk of hospitalization and mortality due to respiratory disease in study IV. A significant increase might have been expected, since several studies have found that cardiovascular comorbidity increases the risk of COPD exacerbations [41-43]. However, other researchers have noted that comorbidity in COPD mainly affects non-COPD–related death and hospitalization [100,137]. The results of this study confirm this finding for comorbid heart disease in patients with COPD.

Comorbid heart disease

Heart disease was defined as having a diagnosis of ischemic heart disease and/or CHF. However, there are indications that CHF has a different impact on clinical outcomes in patients with COPD versus ischemic heart disease [48-50]. Even though ischemic heart disease and CHF often coexist in the same patient, it is worth investigating these two diseases separately in future research.

Recognizing and treating heart disease in patients with COPD

In this real-life study, the diagnosis of chronic heart disease was based on a doctor's diagnosis in the medical records. The participants were not

screened for heart disease at baseline. It is known that heart disease is underdiagnosed in patients with COPD [35,138]. The finding in study III that patients with incident heart disease had the same increased level of dyspnea and the same poor health status as did those with comorbid heart disease at baseline suggests that underdiagnosis also exists in this study population [35,138]. It has previously been shown that worse health status was associated with extra-pulmonary comorbidity in patients with mild to moderate air flow limitation [139]. It is clinically important to be observant for heart disease in a patient whose health status is worse than could be expected according to the airflow limitation. Recognizing comorbid heart disease is important because of the availability of life-saving treatment options and the need for secondary prevention, which has been proven to decrease morbidity and mortality. Herein lies an essential role for primary health care professionals: meeting these patients for follow-up and other intercurrent health problems over many years. This represents one of the core values of general practice, in which disease prevention and health promotion are integrated into daily clinical activities [4].

Sex-related differences

In study I, women were prescribed significantly less RAS inhibitors, in terms of target dose, than were men. The difference could not be explained by age, EF or kidney function. It has been suggested that women have more adverse effects on the recommended medication for CHF, causing them to discontinue their treatment or up titration to target dose and thereby lose its potential benefit [140,141].

A trend was seen in study IV that women with comorbid heart disease had a worse outcome regarding hospitalization and death than men. However, this difference was not statistically significant at interaction analysis. Another study in a Swedish population also found that even though cardiovascular disease was more common among men with COPD, this comorbidity might be of greater importance as a risk factor for death among women [142]. There are indications that women are at higher risk of death from COPD and cardiovascular disease, are undertreated or not benefitting as much as men from advancements in care [143-145]. It is important to have this in mind in daily clinical practice.

Concluding comments

Study I Adherence to guidelines for CHF in primary health care is still suboptimal, particularly regarding medication target dosage. There is also room for improvement in patient education and self-care behavior. Contact with a nurse-led heart failure clinic improves the outcomes, and access to structured multidisciplinary care, even in primary health care, is needed, as is further research on how such care and the therapy guidelines can be adapted to the specific needs of the often older and multimorbid patient population.

Study II Patients with COPD and CHF have similar levels of exercise self-efficacy, symptoms, functional capacity, and health status. This creates the conditions for a beneficial "modeling" effect in a self-management group intended to increase exercise self-efficacy. Low exercise self-efficacy is associated with a high level of symptoms, but not with the specific diagnosis of COPD or CHF. When forming self-management groups, it seems more relevant to consider the level of symptoms than the specific diagnosis.

Studies III and IV Comorbid heart disease contributes to a lower health status and higher level of dyspnea in patients with COPD. However, heart disease does not accelerate the worsening of health status and dyspnea over time. It is important to be observant for undiagnosed heart disease when low health status and a high level of dyspnea cannot be explained by poor lung function alone. Comorbid heart disease in patients with COPD is associated with an increased risk of all-cause hospitalization and mortality, mainly due to an increase in hospitalization and death of cardiovascular and other causes, but not of respiratory disease.

In COPD management in primary health care, it is important to recognize and adequately treat comorbid heart disease.

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Sammanfattning på svenska

Bakgrund

Förbättrade levnadsförhållanden och medicinska kunskaper har bidragit till att befolkningens medellivslängd har stigit . På grund av det har också antalet människor som lever med en eller flera kroniska sjukdomstillstånd ökat. Att ta hand om dessa äldre, multisjuka människor är ekonomisk utmanande för samhället och ställer krav på båda vårdorganisationen och vårdpersonal. Primärvården har de senaste decennierna behövt ta ett större ansvar för att upptäcka, behandla och följa upp denna grupp av patienter.

Allmänläkaren är primärvårdens specialistläkare och arbetar i samverkan med övrig primärvårdspersonal. För att lyckas med denna uppgift måste medicinska bedömningar göras med helhetssyn över patients individuella förutsättningar och flera hälsoproblem hanteras samtidigt, vilket passar bra in i det allmänmedicinska arbetssättet. Förutom följsamhet till nationella och internationella riktlinjer så är det viktigt att involvera patienten i den egna behandlingen och att informera om egenvård. Det är också angeläget att veta hur aktuell samsjuklighet påverkar sjukdomsförloppet.

Avhandlingen handlar om olika aspekter av omhändertagandet av patienter med kroniskt obstruktiv lungsjukdom (KOL) och kronisk hjärtsjukdom i primärvården. De är i sig två stora patientgrupper men även samsjuklighet mellan KOL och hjärtsjukdom är vanligt förekommande.

KOL är en kronisk lungsjukdom som i många fall, men inte alltid, orsakats av tobaksrökning. Tidiga symtom vid KOL är pipande andning och upprepade episoder av hosta med slem. Andra typiska symtom är andfåddhet, trötthet och långvariga eller återkommande förkylningar. I samband med luftvägsinfektioner får KOL-patienterna ofta försämringsperioder, så kallade exacerbationer, som kan bli så allvarliga att det krävs sjukhusinläggning.

Kronisk hjärtsjukdom definieras i denna avhandling som kronisk ischemisk hjärtsjukdom eller kronisk hjärtsvikt.

Patientgruppen med kronisk ischemisk hjärtsjukdom har förträngningar i hjärtats kranskärl som ger bröstsmärtor vid ansträngning. Gruppen inkluderar även besvärsfria patienter som har genomgått behandling för

hjärtinfarkt eller förträngning i kranskärlen med till exempel ballongvidgning eller operation.

Vid kronisk hjärtsvikt förmår hjärtat inte pumpa tillräckligt med blod ut i kroppen. De vanligaste symptomen på hjärtsvikt är trötthet, andfåddhet och bensvullnad. Det finns olika former av hjärtsvikt som klassificeras efter vänsterkammarens pumpfunktion som mäts med ultraljud som procentsatsen av mängden blod som har kommit in i hjärtat som sedan pumpas ut igen. Det kallas vänsterkammarens ejektionsfraktion (EF). Att få rätt mediciner i måldos är särskilt viktigt för gruppen med nedsatt EF. Även vid kronisk hjärtsvikt kan det uppstå sjukhuskrävande försämringsperioder där kroppen samlar på sig vätska i till exempel benen, buken eller lungorna.

En viktig del i egenvård för båda patienter med KOL och hjärtsjukdom är att minska stillasittandet och vara fysiskt aktiv. Fysisk aktivitet och en god kondition skyddar patienter mot försämringar i sin sjukdom, och ökar den hälsorelaterade livskvaliteten. Hälsorelaterad livskvalitet kan man mäta som ”hälsostatus”. För att vara fysiskt aktiv, behöver patienten ha förtroende för sin egen förmåga att kunna vara fysiskt aktiv. Detta förtroende kallas på engelska för ”exercise self-efficacy”.

Syfte

Syftet med denna sammanslagningsavhandling är att studera följsamhet till riktlinjer för kronisk hjärtsvikt i primärvården (delarbete I), patientrelaterade utfallsmått och ”exercise self-efficacy” i KOL och kronisk hjärtsvikt (delarbete II), och påverkan av samsjuklighet i kronisk hjärtsjukdom på andfåddhet, hälsostatus, sjukhusinläggningar och dödlighet i patienter med KOL (delarbeten III och IV).

Delarbete I:

I arbete I undersöktes följsamheten till internationella riktlinjer för utredning och behandling av hjärtsvikt och egenvård i relation till vilken typ av patient det var och vilka kontakter vederbörande haft med vården. Vi vet att följsamhet till riktlinjer och optimal egenvård leder till ökad livskvalitet och minskat behov av sjukhusinläggningar hos patienter med hjärtsvikt.

Alla patienter med en hjärtsviktsdiagnos från tre vårdcentraler i Värmland identifierades och fick en enkät hemskickad med frågor om deras personliga situation och egenvårdsbeteende. Av de 155 (63% av de tillfrå-

gade) patienter som svarade på enkäten gjordes en journalgranskning för att se vilka utredningar som utförts, vilken medicinering de fått förskrivit och vilka vårdkontakter de hade.

Det visade sig att cirka fyra av fem patienter hade fått diagnosen efter analys av de av riktlinjerna rekommenderade blodprov och en ultraljudsundersökning av hjärtat hade gjorts. De flesta patienter med nedsatt EF fick rätt läkemedelskombination men det var få som fick det i tillräcklig hög dos. Cirka en tredjedel av patienterna angav att de inte visste att de hade en hjärtsviktsdiagnos. Det fanns även utrymme för förbättring vad gäller patientutbildning kring egenvård. Hos de patienter som hade varit i kontakt med en sjuksköterskeledd hjärtsviktsmottagning följdes riktlinjerna i högre utsträckning än hos de som inte hade träffat en hjärtsviktssjuksköterska.

Slutsatsen var att följsamhet till riktlinjerna vad gäller utredning och behandling hade förbättrats jämfört med tidigare studier utförda i Sverige och i Europa, men att den fortfarande inte är tillräcklig, särskilt när det gäller måldoser för läkemedel. För att förbättra patienternas egenvård och öka följsamheten till behandling behövs specialiserade hjärtsviktsmottagningar i primärvården.

Delarbete II:

Arbete två undersökte skillnader och likheter mellan patienter med KOL och hjärtsvikt vad gäller ”exercise self-efficacy”, hälsostatus, uppmätt fysisk förmåga och symptom och hur dessa faktorer hänger ihop och påverkar varandra. Syftet med detta var att undersöka om det kan vara möjligt att ha patienter med olika diagnoser i samma patientutbildningsgrupp med målet att öka deras ”exercise self-efficacy”.

En patientenkät fylldes i av 150 patienter med kronisk hjärtsvikt och/eller KOL. Enkäten bestod av frågor om deras personliga situation och innehöll frågelistor som mätte deras hälsostatus, smärta, trötthet, andfåddhet, psykiska besvär och ”self-efficacy” för att utföra fysisk aktivitet. Den fysiska förmågan mättes med ett test av gångsträckan under 6 minuter.

Det visade sig att nivån på ”exercise self-efficacy”, hälsostatus, den fysiska förmågan och symptom var jämförbara mellan patienter med KOL och kronisk hjärtsvikt. Vid högre grad av andfåddhet, nedstämdhet, ångest och smärta minskade ”exercise self-efficacy” oberoende av diagnos, kön eller ålder.

Slutsatsen var att det går att forma gemensamma utbildningsgrupper med målet att öka ”exercise self-efficacy” baserat på symtom snarare än på vilken sjukdom man har. Det behövs dock mera forskning för att se hur detta koncept skall fungerar i praktiken.

Delarbete III:

Arbete tre undersökte hur samsjuklighet i hjärtsjukdom påverkar graden av andfåddhet och hälsostatus hos patienter med KOL över en tidsperiod på sju år.

För detta arbete fanns ett slumpvist urval av 1584 patienter med KOL från 56 vårdcentraler och 14 sjukhus i Mellansverige, den så kallade PRAXIS I studien. År 2005 svarade 1089 (69%) på en enkät med frågor om grad av andfåddhet och hälsostatus. Det gjordes även en journalgranskning för att samla data om samsjuklighet i hjärtsjukdom och övriga faktorer som kan påverka andfåddhet och hälsostatus. Under 2012 fick de patienter som fortfarande levde en ny enkät hemskickade. Totalt 495 patienter svarade på alla frågor både 2005 och 2012 och inkluderades i studien.

Patienter som hade både KOL och hjärtsjukdom hade en högre grad av andfåddhet och sämre hälsostatus jämfört med patienterna som hade KOL utan hjärtsjukdom. Andfåddheten och hälsostatus försämrades lika mycket över tid för båda grupper. Gruppen som fick en hjärtsjukdomsdiagnos mellan 2005 och 2012, hade redan mera besvär av andfåddhet och sämre hälsostatus år 2005, innan diagnosen ställdes.

Slutsatsen var att samsjuklighet i hjärtsjukdom ökar graden av andfåddhet och minskar hälsostatus i patienter med KOL men skillnaden mellan grupperna ökar inte över tid.

Delarbete IV:

Arbete fyra undersökte hur samsjuklighet i hjärtsjukdom påverkar sjukhusinläggningar och dödlighet hos patienter med KOL över en period om 15 år.

Detta arbete använde samma patientgrupp och data från 2005 som delarbete III. Information från Patientregistret användes för att jämföra antalet inläggningar och inläggningsorsak mellan patienter med KOL med och utan hjärtsjukdom. Data från Dödsorsaksregistret användes för att göra överlevnadsanalyser för att se hur samsjuklighet i hjärtsjukdom påverkade dödlighet och dödsorsak i denna patientgrupp.

Det visade sig att patienter med samsjuklighet i hjärtsjukdom hade högre risk att bli inlagda på sjukhus. Dödligheten var också högre i denna patientgrupp. Patienter med samsjuklighet hade en högre risk för inläggning och död i hjärtkärlsjukdom och andra orsaker, men inte för lungsjukdom. Många patienter utan hjärtsjukdom i studiens början fick en diagnos på hjärtsjukdom mellan studiens start och slut.

Slutsatsen var således att samsjuklighet i hjärtsjukdom hos patienter med KOL ökar risken för sjukhusinläggningar och dödlighet, vanligen orsakad av hjärtkärlsjukdom och andra orsaker. Samsjukligheten ökar inte risken för sjukhusinläggning och dödlighet på grund av lungsjukdom.

Resultaten från arbete IV och III påvisar att vid omhändertagandet av patienter med KOL i primärvården är det viktigt att upptäcka hjärtsjukdom och behandla detta adekvat.

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