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## Patient-reported outcomes in patients with heart failure

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Imke H. Kraai

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Kraai, IH

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# Patient-reported outcomes in patients with heart failure

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# General introduction and outline of the thesis

Patient-reported outcomes in patients with heart failure



## Patient-reported outcomes in patients with heart failure

### **Introduction**

How patients perceive their disease is increasingly recognized as an important aspect in the treatment trajectory for chronic diseases. In the search for new interventions to treat chronic diseases the focus was in the early days (and even nowadays) mainly on ways to reduce mortality and morbidity and to make efficient use of healthcare resources, which are mainly reflected by the number of (re)hospitalizations. The perception of the patient suffering from a chronic disease, the so-called patient-reported outcome (PRO), was rarely included in the evaluation of new interventions. Nowadays, the European Society of Cardiology, the American Heart Association and the United States Food and Drug Administration also recommend the use of patient-reported outcomes in the evaluation of interventions.<sup>1-4</sup> Gaining insights into patient-reported outcomes is important with respect to providing personalized care on a patient level, optimizing care on a population level and identifying the most appropriate patient-reported outcomes for clinical trials.

### **Patient-reported outcomes**

Patient-reported outcomes are defined as: “any report of the status of a patient’s health condition that comes directly from the patient without interpretation of the patient’s response by a clinician or anyone else.”<sup>4</sup> The term patient-reported outcomes is an umbrella term that encompasses any outcome derived from patient reporting,<sup>5,6</sup> such as health-related quality of life, number and severity of symptoms, physical performance,<sup>4</sup> patient satisfaction, patient preferences,<sup>7</sup> perceived control,<sup>8</sup> disability or handicap, adverse events, treatment tolerability, treatment satisfaction<sup>9</sup> and activities of daily living.<sup>5</sup> Patient-reported outcomes can be used to measure the effectiveness of a treatment on the severity of a symptom or sign, the status of the disease from the patient’s perspective, the patient’s level of functioning, the patient’s satisfaction with the treatment or the health status, the degree of health-related quality of life, the degree of disability, or the tolerability of the treatment.

The safety of an intervention can be measured by patient-reported outcomes as well, for example, by measuring the symptoms and signs experienced by the patient. By using patient-reported outcomes in clinical trials, the effect of interventions can be assessed from

a patient's perspective. This approach is particularly useful in interventions aimed at improving symptoms or functional status.<sup>10</sup>

### **Heart failure**

Heart failure is one of the most prevalent chronic diseases among older adults. Patients with heart failure have to cope with a chronic and debilitating condition, often characterized by periods of worsening symptoms and hospitalization.<sup>11</sup> The prognosis is poor because heart failure generally cannot be cured and can only be managed by non-pharmacological treatment and/or pharmacological treatment, sometimes combined with surgery or implantation of a pacemaker or other device.

Although survival after the diagnosis of heart failure has improved in the past 30 years, the prospects of patients with heart failure remain poor, and no less than 50% of patients with heart failure will die within four years after diagnosis.<sup>11,12</sup> Heart failure affects about 10% of men and 8% of women over the age of 60 years and the prevalence increases with age.<sup>12</sup> The prevalence varies between 2 and 3% and rises sharply at around 75 years of age, resulting in a prevalence of between 10 and 20% in patients aged 70 to 80 years.<sup>11</sup> In the last two decades, the heart failure population changed to a population with a higher percentage of very elderly patients, who have a higher number of comorbidities.<sup>13</sup> As a result, the care for patients with heart failure has also changed. The first step towards organizing the treatment and care more efficiently involved the establishment of specialized heart failure outpatients clinics that are characterized by a strong collaboration between heart failure nurses and cardiologists<sup>14,15</sup> and the introduction of so-called Disease Management Programs. These are multidisciplinary intervention designed to improve quality and cost effectiveness of care, using a systemic approach and employing multiple treatment modalities.<sup>16,17</sup> The use of a Disease Management Program in heart failure clinics is currently part of standard care for patients with heart failure in several European countries.<sup>18</sup>

Nowadays the European Society of Cardiology and American Heart Association also recommend careful monitoring of heart failure patients by means of telephonic assessments or telemonitoring, in addition to regular visits to the outpatient clinic.<sup>19</sup> Telemonitoring makes it possible to collect information about the patients' condition, for instance, blood pressure, heart rate, and weight, on a frequent basis without the patient having to leave his or her

home. This information can be used to treat the patient more effectively, to prevent hospitalization, and to improve the prognosis.

### **Patient-reported outcomes in heart failure trials**

Two types of end points are considered to be clinically meaningful in the evaluation of treatment in patients with heart failure. The first type of endpoint evaluates changes in clinical status, for example, symptoms, health-related quality of life, well-being and functional capacity. The second type of endpoint evaluates the risk of a major clinical event,<sup>20</sup> for example, mortality, death or hospitalization. Until recently, and despite the treatment objectives, cardiovascular trials have been primarily oriented at endpoints that evaluate the risk of a major clinical event. However, it is clear that health-related quality of life in patients with heart failure is seriously reduced compared with both a normative population<sup>21</sup> and patients suffering from other diseases.<sup>22</sup> From a patient's perspective, the treatment of heart failure should be primarily aimed at the relief of symptoms and improvement in health-related quality of life.<sup>11</sup>

In 2001, Packer proposed a clinical composite score that combines both types of endpoints.<sup>20</sup> This clinical composite score classifies each randomized patient as improved, unchanged, or worse, depending on the clinical response during the trial and the clinical status at the end of the trial.<sup>20</sup> The use of composite endpoints is recommended by the European Society of Cardiology Heart Failure Association.<sup>2</sup> A derivative of the composite score proposed by Packer is used in the African-American Heart Failure Trial (A-HeFT).<sup>23,24</sup> The primary efficacy variable in the A-HeFT was a composite score of clinical outcomes including death, first readmission for heart failure, and change in health-related quality of life. In this scoring system, a sum score was calculated for each component, depending on whether or not a given event was experienced by the patient. This makes it possible to assign a numeric value to each study subject so that all patients contribute directly to the total group score.<sup>23</sup> The composite endpoint of the A-HeFT was also used in the Innovative ICT guided disease management combined with telemonitoring in outpatient clinics for chronic heart failure patients (IN TOUCH) trial.<sup>25</sup>

The prevalence of patient-reported outcomes, such as health-related quality of life, in contemporary cardiovascular trials is 16%.<sup>10</sup> This percentage is on the rise after the US Food and Drug Administration recommended its use in medical product development<sup>4</sup> and because

of the aforementioned recommendations by the European Society of Cardiology<sup>2</sup> and the American Heart Association.<sup>1</sup> Furthermore, knowledge about patient-reported outcomes is vital for the delivery of optimal and personalized health-care to patients with heart failure. Use of patient preferences makes it possible to assess preference regarding quality of life or longevity. Research has shown that older patients may not tolerate or benefit from guideline-recommended heart failure therapies.<sup>26</sup>

Therefore, it is important that the health-care provider knows the preferences of a patient with respect to quality of life or longevity, assesses and communicates prognoses, and discusses goals of care so as to deliver optimal healthcare to a patient.<sup>11,27</sup> In addition, from the perspective of healthcare policy and research, which use patient-reported endpoints, knowledge of patient preferences regarding different interventions is an important component of rational decision making. These insights into the preferences of patients enable open and personalized discussions of preferences in treatment and care decisions, and can guide the future development of more patient-centred care.

## Aims of this thesis

Research on new interventions generally uses traditional outcomes such as hospitalization and mortality. However, the question is whether patients with heart failure actually consider these traditional outcomes to be important or that they perceive other outcomes to be equally or even more important.

A key challenge in heart failure care is to understand and to find ways to help patients with heart failure to live a normal life within the limits imposed by their disease. Hence, knowledge of which treatment goals patients with heart failure prefer is vital. This knowledge can be used to identify the most appropriate patient-reported outcomes for clinical trials, to optimize care on a population level, and to personalize heart failure care on a patient level. This thesis aims to investigate the use of patient-reported outcomes in patients with heart failure and the perception of these outcomes by the patients themselves.

### **The specific aims of this thesis are:**

- (1) To explore the preferences of patients with heart failure regarding quality of life versus longevity and to research patients' most important treatment goals. This is studied in chapter 1 and 2.
- (2) To explore the impairments in patients with heart failure and their effects on health-related quality of life. This is reported in chapter 3.
- (3) To identify other potential outcomes that influence health-related quality of life in patients with heart failure and that can be measured by new interventions. This is studied in chapter 4 and 5.
- (4) To explore the measurement of patient satisfaction with non-invasive telemedicine and to describe how satisfaction can be measured within a specific framework. This is described in chapter 6.
- (5) To explore the effect of telemonitoring in addition to an ICT-guided disease management system in patients with worsening heart failure; results of the IN TOUCH study. This is described in chapter 7.

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