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Assessing Symptom Burden and Health-Related Quality of Life in patients living with arrhythmia

and

ASTA

Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia

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To Hanna, David & Håkan

Ju mer man tänker, ju mer inser man att det inte finns något enkelt svar

Nalle Puh

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ABSTRACT

Health-Related Quality of Life (HRQOL) can be negatively affected in patients living with arrhythmias and many patients experience a pronounced symptom burden. The arrhythmia can cause both uncertainty and limitations, including interference with work, reluctance to perform and plan for leisure activities and leading to self-imposed restrictions in daily life situations. There are patients striving to find strategies to manage the arrhythmia and for some this can become the focus in their lives. Treatment options are often a choice between pharmaceuticals and radiofrequency ablation (RFA) where RFA is an option for many arrhythmia-patients to be cured. In the care of arrhythmia-patients it is of great importance to combine objective examinations with patient-reported outcomes (PROs) to achieve patient's own experiences of treatment efficacy and arrhythmias interference in daily life situations.

The overall aims of this thesis were to assess symptom burden and HRQOL in patients with arrhythmias and to develop and validate an arrhythmia-specific questionnaire, suitable for most arrhythmia-patients.

Studies I and II were single-centre studies including patients referred for RFA, with two different arrhythmia diagnoses. Assessments of patient-reported outcomes (PROs) concerning HRQOL were performed using two questionnaires, SF-36 and EQ-5D (I-II). Further, patients were asked some disease-specific questions (I). Study I describes assessments before the RFA treatment and Study II the follow-up assessments at three and twelve months after RFA. Patients' scoring of HRQOL was compared to age and gender matched reference groups before and after RFA (I-II). Studies III and IV describe the development and validation of a disease-specific questionnaire ASTA (Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia) assessing symptom burden and HRQOL. Studies III and IV were multicentre studies. Patients planned for DC-conversion, AF patients seeking emergency care and those with different forms of arrhythmias referred for RFA were included.

Patients scored significantly lower HRQOL in seven of SF-36's eight scales compared to the age and gender matched reference groups before RFA treatment. Frequent arrhythmia attacks had a great negative impact on HRQOL, and female gender and older age were factors contributing to worse HRQOL (I). Treatment with RFA restored the patients' HRQOL. Most positive effects were seen at three months follow-up. One year after treatment patients and the matched reference group scored their HRQOL to a similar level, assessed with SF-36 and EQ-5D index (II). The validated ASTA questionnaire was found to have good psychometric properties. Construct validity was confirmed with sufficient levels of item-total correlations in the ASTA symptom burden scale and HRQOL scales. The dimensionality of the ASTA HRQOL scale was established with confirmatory factor analysis, supporting a physical and a mental subscale. The internal consistency, demonstrated with Cronbach's alpha (α), was satisfactory for the ASTA symptom burden scale and the ASTA HRQOL scales, varying from α 0.79 to α 0.91 (III-IV).

Results from the studies in this thesis confirmed how negatively affected the arrhythmia-patients can be with a pronounced symptom burden and impaired HRQOL. Treatment with RFA was demonstrated to restore the patients HRQOL to an equal level of that of the matched reference group. PROs are important to take into consideration in the care of arrhythmia-patients, to achieve the patients' subjective experiences of their daily life situation.
To the best of our knowledge ASTA is the first arrhythmia-specific questionnaire assessing symptom burden and HRQOL, suitable for most arrhythmia forms. The newly validated ASTA questionnaire can be an important contribution to assessment of PROs in arrhythmia-patients.

Keywords
Arrhythmias, Symptom burden, Health-Related Quality of Life, Patient-reported outcomes, Validation, Disease-specific questionnaire

LIST OF PAPERS

I. Ulla Walfridsson, Anna Strömberg, Magnus Janzon and Håkan Walfridsson. Wolff-Parkinson-White Syndrome and Atrioventricular Nodal Re-Entry Tachycardia in a Swedish Population: Consequences on Health-Related Quality of Life
Pacing Clin Electrophysiol 2009, 32(10):1299-1306

II. Ulla Walfridsson, Håkan Walfridsson, Kristofer Årestedt and Anna Strömberg. Impact of radiofrequency ablation on health-related quality of life in patients with paroxysmal supraventricular tachycardia compared with a norm population one year after treatment
Heart & Lung 2011, 40(5):405-411

III. Ulla Walfridsson, Kristofer Årestedt and Anna Strömberg. Development and validation of an Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmias with focus on symptom burden and patient-reported symptoms
(Submitted)

IV. Ulla Walfridsson, Anna Strömberg and Kristofer Årestedt. Development and validation of an Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmias with focus on Health-Related Quality of Life
(Submitted)

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ABBREVIATIONS

AF	Atrial fibrillation
AFL	Atrial flutter
ASTA	Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia
AVNRT	AV-Nodal reentry tachycardia (Atrioventricular nodal reentry tachycardia)
EQ-5D	EuroQol five dimensions and visual analogue scale
EQ-5D index	EuroQol five dimension summarized index
EQ VAS	EuroQol visual analogue scale
FAT	Focal atrial tachycardia
HRQOL	Health-Related Quality of Life
PROs	Patient-reported outcomes
PSVT	Paroxysmal supraventricular tachycardia
PVCs	Premature Ventricular Contractions
QOL	Quality of Life
RFA	Radiofrequency catheter ablation
SCL	Symptom Checklist; Frequency and Severity Scale
SF-36	MOS 36-item Short-Form Health Survey
SVT	Supraventricular tachycardia
VT	Ventricular tachycardia
WPW	Wolff-Parkinson-White syndrome

INTRODUCTION

To live with a heart rhythm disturbance (arrhythmia) can have a pronounced negative impact on a person's entire life situation. Arrhythmias are relatively common and in their most common form estimated to be present in 1-2 % in the population, with an increasing prevalence in older ages. Patients can have frequent attacks with symptoms varying from mild palpitations to dizziness, anxiety, shortness of breath and sometimes even syncope.[1-7] The often unpredictable nature of arrhythmia can lead to experiences of both uncertainty and feelings of incapacity, where it can be of great importance to find self-management strategies and causative factors to prevent new attacks.[8-9] Suffering from arrhythmia can negatively affect physical, mental as well as social aspects in a patient's daily life leading to an impaired Health-Related Quality of Life (HRQOL).[10-14] Presence of arrhythmia can cause both short-term absences from work as well as sick-leave, thereby with negative economic consequences. [15-16] There are patients reluctant to plan and perform leisure activities in fear of arrhythmia recurrence and those afraid of driving alone, leading to self-imposed restrictions. [6,17]

Cited from patients:

"I´ll never drive alone nowadays, and if it is possible I choose to not drive on motorways"

"I´m afraid of having intimacy with my partner because I´ll try to avoid anything that might trigger the arrhythmia"

"I´m so glad that I reached our driveway before I fainted in the car"

Long term strategy is often a choice between pharmacological treatment and radiofrequency catheter ablation (RFA). Pharmacological treatment can be an option, but it is less effective and can cause side effects. RFA nowadays is the treatment of choice for many patients suffering from arrhythmia. [1-2,4,10,13,18-23] In the care of arrhythmia-patients of great importance are follow-up strategies combining objective measurements, for example ECG, with evaluations of

patients' own experiences, i.e. assessments of patient-reported outcomes (PROs). PROs can contribute with valuable information before, during and after a treatment and cannot be replaced by solely objective registrations. Assessing PROs concerning symptom burden and HRQOL due to a certain disease requires questionnaires validated in the targeted patient population. [24-28]
To the best of my knowledge there has not been such a questionnaire available exploring both symptom burden and HRQOL in one questionnaire suitable for most forms of arrhythmias.

AIMS OF THE THESIS

The overall aims of this thesis were to assess symptom burden and Health-Related Quality of Life in patients with arrhythmias and to develop and validate an arrhythmia-specific questionnaire, suitable for most arrhythmia-patients.

The specific aims of the studies were:

I. To describe and compare Health-Related Quality of Life in patients suffering from AV- Nodal reentry tachycardia or Wolff-Parkinson-White syndrome in patients referred for radiofrequency ablation compared to age and gender matched reference groups.

II. To evaluate the impact of radiofrequency ablation on Health-Related Quality of Life in patients with paroxysmal supraventricular tachycardia compared with a norm population one year after treatment.

III. To develop and validate a disease-specific symptom burden scale for patients with different forms of arrhythmias i.e. supraventricular arrhythmias including atrial fibrillation and ventricular arrhythmias and to describe patient-reported arrhythmia symptoms.

IV. To develop and validate a disease-specific questionnaire evaluating Health-Related Quality of Life in patients with different forms of arrhythmias i.e. supraventricular arrhythmias including atrial fibrillation and ventricular arrhythmias.

BACKGROUND

Arrhythmias

Definition, prevalence and diagnosis

There are several forms of arrhythmias originating from the atria, supraventricular tachycardia (SVT), and some from the ventricles. In these, mostly rapid arrhythmias, i.e. tachycardia (heart rate ≥100 beats/minute), there are one or more mechanisms involved with impulse initiation or abnormalities with the impulse conduction.[2] SVT often appears with recurrent, rapid attacks (paroxysmal supraventricular tachycardia (PSVT)), but can sometimes be persistent. The prevalence of PSVT is estimated to be approximately 0.5 – 1 %. [2,5] The different supraventricular arrhythmias are AV-Nodal reentry tachycardia (AVNRT), Wolff-Parkinson-White-syndrome (WPW), focal atrial tachycardia (FAT) atrial macro-reentry, atrial flutter (AFL) and the most common form; atrial fibrillation (AF). [2,4] AF is seldom present in younger ages but with a rapidly increasing prevalence in older ages, estimated to be present in approximately 10 % or more in ages of 80 years and older.[4-5]
Arrhythmias originating from the ventricles are either ventricular tachycardia (VT) or frequent and premature ventricular beats (PVCs). [1,5]

The arrhythmia diagnose is usually confirmed by an electrocardiogram (ECG). Sometimes it can be difficult to discriminate between different forms of arrhythmias, and in some patients the definite diagnose is achieved during an invasive electrophysiological study (EP-study).

AV-Nodal reentry tachycardia and Wolff-Parkinson-White syndrome

AVNRT is the most common form of PSVT with a higher incidence in female patients, in contrast to WPW more commonly seen in male patients. Patient in

both groups are often rather young and healthy. [2,29-30] The heart rate during an attack of AVNRT may vary between approximately 140-250 beats per minute, where female patients have been shown to have more rapid arrhythmias than men.[31] The heart rate during attacks of WPW tachycardia is similar to those due to AVNRT. Both arrhythmias are characterized by reentry circuits with regular QRS-complexes. [2] AVNRT's electrical reentry circuit involves the AV-node, sometimes described to be due to so-called "dual AV-nodal physiology". The WPW-syndrome is due to an accessory pathway connecting the atrium to the ventricle, using the specialized conduction system in the reentry circuit. [2,29-30] Both forms are usually judged to be not life-threatening but sometimes in WPW patients during AF (preexcited AF) this can lead to a high ventricular rate even degenerating into ventricular fibrillation.[2,30,32]

Atrial fibrillation

AF is the overall most common form of arrhythmia, a supraventricular arrhythmia, where men are more often affected. [4-5,33-34] The heart rate is irregular, mostly with narrow QRS-complexes and where the heart rate can vary from being rapid to slow [4-5]. There are different forms of AF: AF in recurrent attacks named paroxysmal AF, AF attacks needing medical intervention to be interrupted and called persistent AF, long standing persistent and/or permanent AF. [4] Patients with AF are often older and with more concomitant diseases.[4-6,33,35] A structural remodeling in the atria leads to electrical dissociation and can thereby initiate AF, with small and multiple reentry circuits, stabilizing the arrhythmia. The mechanism behind AF onset is usually attributed to rapid electrical discharges within the pulmonary veins.[4,34, 36] AF is an independent risk factor for thrombo-embolic stroke, this irrespective of the form of AF.[4-5,33,37]

Other arrhythmias

Atrial flutter

AFL is an organized atrial rhythm, often with an atrial rate varying from approximately 250 to 320 beats per minute and with varying AV-nodal conduction. [2,5] This patient group is rather similar to the AF patients, often

older, mostly men and often with concomitant diseases.[5-6,38] There are AFL patients who experience an extremely rapid heart rate during tachycardia with 1:1 AV-conduction that can lead to life-threatening symptoms. A common combination in a patient with AFL is also to have AF, as seen in 25-35 % of the patients. The risk for stroke in AFL patients is comparable to the risk in AF patients. [2,5,34-35] The macro-reentry circuit in "typical" AFL is present in the right atrium and the arrhythmia can occur in attacks or in persistent form.[2,5,39]

Other atrial macro-reentry arrhythmias

There are other similar atrial arrhythmias, named atrial macro-reentry arrhythmias, most often seen after RFA treatment for AF but also occurs spontaneously usually due to scaring within the atria or as a result of surgical procedures. This atrial arrhythmia is either present as a micro-reentry or with a macro-reentry mechanism. [40-41]

Focal Atrial Tachycardia

FAT is characterized by a regular activation from areas (foci) in the atrium and with a heart rate between 100 and 250 beats per minute.[2] This arrhythmia usually occurs with a "warming-up" phenomenon, meaning an accelerating start without a distinct onset. This is normally a benign form of arrhythmia and can be present either in the form of a paroxysmal or a persistent tachycardia. When it is present in its sustained form it can cause dilated cardiomyopathy. [2,42-43] FAT is a special form of arrhythmia in that patient sometimes can have a spontaneous remission of the tachycardia. [42-43]

Ventricular arrhythmias

Ventricular arrhythmias, often tachycardia (VT), can exist with or without (idiopathic VT) an underlying structural heart disease. Instead of having tachycardia attacks there are other patients with ventricular arrhythmias that suffer from frequent, repetitive, symptomatic and premature ventricular contractions (PVCs). The prognosis for patients with ventricular arrhythmias is

dependent on the presence or absence of an underlying heart disease, with a good prognosis when without an underlying heart disease.[1,5,44] After a myocardial infarction reentry circuits can occur due to ventricular scars, while in idiopathic VTs the arrhythmia mostly has a focal origin.[1,44]

Treatment options for arrhythmia-patients

Initially many patients start with pharmacological therapy. Pharmacological treatment is not curative but for some this can be effective and reduce the symptom burden. [19,45] Unfortunately, for several of the anti-arrhythmic drugs available there is a lack of sufficient efficacy and therapy with drugs can cause side-effects, these both disabling and sometimes life-threatening. [10,19,33]

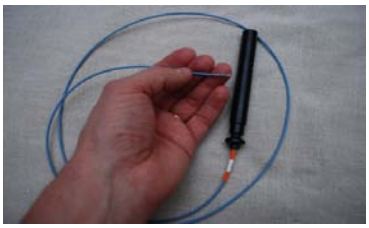
In patients with persistent arrhythmias such as AF and AFL, treatment with direct current cardioversion (DC-conversion) can be a treatment of choice. [4-5,34] Mostly this interrupts the sustained arrhythmia, but, it can be demanded repeatedly when the arrhythmia reoccurs.
A short duration of arrhythmia both increases the possibility to achieve sinus rhythm at the conversion and to maintain it, compared to those with longer durations.[5,46] DC-conversion is a "here and now" option. The patient receives a short sedation during the DC-conversion shock and can usually leave the hospital after some hours. This is routinely performed at many hospitals and is an intervention with a low risk for complications, when necessary precautions are taken in preventing thrombo-embolic events. [4-5]

For many arrhythmia-patients treatment with RFA has become a suitable and curative alternative and for some arrhythmias this is now a first line therapy. RFA is an invasive catheter method performed in a special electrophysiological laboratory. The method has been extensively developed during the last decades. Catheters are moved from the groin to the patients' heart. The electrophysiological properties are examined and the arrhythmia diagnose confirmed. Radiofrequency energy is the most commonly used method when ablating arrhythmia-patients, but the cryo-technique where the tissue is frozen to -70-80 degrees is also used.[1-2,4-5,20,22-23,40,47-51] There are different RFA techniques depending on the underlying arrhythmia and some patients receive a pacemaker before the ablation is performed (e.g. His-bundle ablation in AF

patients). [5,52] RFA can be performed as an out-patient-clinic visit during a day or with the patient admitted to hospital for a few days, depending on the type of arrhythmia. The risk for complications with RFA treatment is low and dependent on the underlying arrhythmia and on concomitant diseases.[5,53-54]

Electrophysiological laboratory

RFA catheter



Most interventions ease the patient's symptom burden and improve the HRQOL with most pronounced positive effects seen for RFA treatment. [10-11,13,18,55-56]

In highly symptomatic and/or drug refractory AF patients, there are options to treat with either thoracic epicardial RFA or cryoablation or with open-heart surgery, the MAZE technique. [57-59]

Symptoms and symptom burden

The word symptom originates from the Greek word "symptoma," and means "anything that has befallen one."[60] Symptoms are subjectively experienced responses from a patient to a disease, injury, a physical disturbance or produced by treatment side-effects and can cause changes in HRQOL. Conversely from signs that can be observed from others, symptoms can only be known from reports from the patient herself/himself.[60-62] The main goal of a certain therapy can be either to achieve cure or symptom relief. Therefore assessment of patients' symptom burden is of great importantance.[26-28,63]
The concept symptom burden can be described as a summary of the severity and impact of symptoms, reported by a number of patients with a specific disease or due to a certain treatment. It is not only measurements of HRQOL that can be divided in physical and mental domains, sometimes also symptoms have been described to be either physical, psychophysical (more associated with mental health) or emotional (frustration, worry), where the classification relates to the origin of the symptoms. [60,62,64] Commonly included in symptom measurements are evaluation of frequency, intensity, distress but also the duration of the

symptoms. [33,64-66] There are factors to take into consideration concerning what might influence a person's experiences, interpretations and evaluations of their symptoms, such as individual and environmental factors. Severity of symptoms, the impact, timing and if the person/patient suspects any particular causes, can be of interest to examine.[60,64]

Health, Quality of Life and Health-Related Quality of Life

Health and Quality of Life

Stated by the World Health Organization (WHO) health is *"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"*.[67] At the time for the development of this definition the new aspect was that it took a holistic view of health and suggested that health is more than the absence of a disease.[68] Health is one important aspect of Quality of Life (QOL).

QOL has been defined by WHO as *"individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"*. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment. [67] QOL is historical and has been with us since the days of Aristotle and in the 1950s the QOL concept was stated to be what was important in life.[68-69]
Definitions of QOL have generated controversies over the years, with several researchers giving their definition. QOL is about the goodness of life and emphasize both happiness and satisfaction. In the concept QOL several domains are included: physical and material well-being, personal fulfillment with recreation, educational and economic status and aspects about living standard, cultural, relations, political freedom, public safety as well as spiritual issues. [61,68,70] The challenge for healthcare providers is to be aware that satisfaction with health is solely one of the components/domains in satisfaction with life and QOL. [68]

Thus, with the ambition to focus on how the effects of health, illness and different treatments influence a person's QOL, i.e. to narrowing QOL, to reduce ambiguity the concept Health-Related Quality of Life (HRQOL) was introduced. [64,71]

Health-Related Quality of Life

The HRQOL concept has no clear definition and it is ambiguous what aspects of QOL that should be included. There are difficulties to make clear distinctions between the two multidimensional concepts QOL and HRQOL, but HRQOL has been described to involve concerns related to health and daily life such as physical functioning (physical), psychological well-being (mental) and social functioning (social aspects).[24,62,64,71-72]

HRQOL is a subjective measure of an individuals' perception of a treatment's or a disease's impact on their health status. Assessment of HRQOL is a valuable complement to clinical outcomes in order to achieve information from a patient perspective and it has become an increasingly important outcome measurement often also warranted from a societal perspective.[24-25,27,68,71-72] HRQOL measurements have been increasingly used in clinical trials to achieve information about treatment outcomes after different healthcare interventions. Evaluations of HRQOL should be possible to interpret in clinical practice when making treatment decisions as well as to provide valuable self-experienced patient information. HRQOL can provide useful information when there is a choice between different treatments, expected to be equivalently effective, and concerning late coming problems in patients suffering from chronic diseases. [24-25,73] With new medical technologies and limited economic resources there is a need for documentation of treatment outcomes, to ensure treatment effectiveness. It has been requested by regulatory authorities for making policy decisions as well as from pharmaceutical companies to evaluate treatment strategies and side-effects. [24,62,68]

Assessment of symptom burden and Health-Related Quality of Life in arrhythmia-patients with patient-reported outcomes

In the care of arrhythmia-patients it is essential to explore the patient's experiences and effects of living with arrhythmia. Patient-reported outcomes (PROs) are requested and can be achieved by, for example, interviews, and diaries or by questionnaires.[24-25,60,74] In healthcare we can register signs of illness or a disease by objective measurements but to gain a deeper understanding of the patient's experiences of a certain disease, there is a need for PRO assessments. PROs are the subjective description of the patient's self-experienced life situation, giving valuable information and cannot be replaced by only objective examinations. Assessment of symptom burden and HRQOL can be the primary outcome during a treatment or after an intervention. [24-25,28,60] There are arrhythmia-patients with barely any signs of arrhythmia at all but mostly the patients have a distinct onset of the arrhythmia and some with the presence of disabling and handicapping symptoms such as anxiety, shortness of breath, near syncope and syncope. [1-2,4,7,13]
Symptom burden can be pronounced, and can thereby negatively influence different domains in life, leading to an impaired Health-Related Quality of Life (HRQOL). [3,7,10,12-14] Impaired HRQOL can be demonstrated in younger and healthier arrhythmia-patients as well as in the older patients with more concomitant diseases. [10-11,13] The usual form of obtaining assessments of symptom burden and HRQOL are by using questionnaires and there are two basic categories of questionnaires**:** generic and disease-specific questionnaires. [24,71]

Generic questionnaires

Generic questionnaires can provide health status measures for example in a general population or in comparisons between different diseases, where it is not relevant to use a disease-specific questionnaire. Two well-known and widely used questionnaires are the MOS 36-item Short-Form Health Survey (SF-36) and EuroQol five dimensions and visual analogue scale (EQ-5D). Both these generic questionnaires assess HRQOL and can be used for the purpose of exploring Quality Adjusted Life Years (QALYs). Single item measurement is an

alternative but can be compromised both concerning reliability and the precision of the measurement. [24,75-81] Using generic questionnaires in evaluations of HRQOL are useful when comparing patients with different diseases but less sensitive to specific concerns that can be affected by a specific disorder. [25]

Disease-specific questionnaires

Disease-specific questionnaires focus on a certain disease's aspects and impact on HRQOL. Probably the most commonly used questionnaire in arrhythmia-patients is a checklist**:** Symptoms Checklist; Frequency and Severity Scale (SCL version 3) evaluating arrhythmia-related symptoms concerning the symptoms frequency and grade of severity. SCL has been used in different forms of arrhythmias but most often in AF patients.[10,82-83]
There are some new arrhythmia-specific questionnaires available and validated since the start of the development of the ASTA questionnaire (Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia). Some of which include most arrhythmia-patients except AF patients or solely including patients with AF. Others are very briefly evaluating the patients' situation or developed solely for the assessment of symptoms or HRQOL. [65-66,84-87] (Table 1)

There is one protocol for PROs to quantify symptoms in SVT patients, not yet validated. Most scales/questionnaires are used in AF patients. Some are for clinicians' use, developed for evaluation and classification of arrhythmia-related symptoms in AF patients where one is the EHRA- classification (European Heart Rhythm Association), also for AF patients. [33,88-92]

There was a lack of an arrhythmia-specific questionnaire, assessing both symptom burden and HRQOL, suitable for most forms of arrhythmias. After the data collection period for study I and II were finalized, we saw a need for a disease-specific questionnaire to enable assessments of arrhythmia**'**s symptom burden and the influence on our patients' daily life. In a previous project we used the SCL after translation to Swedish. The fact that this checklist only evaluates symptoms, not HRQOL, became the starting point for the development of the ASTA questionnaire.
So, to the best of knowledge, there is still no other questionnaire for PROs such as ASTA; developed and validated with separate parts exploring symptom burden and HRQOL, in a questionnaire suitable for most arrhythmia-patients.

Table 1 Description of arrhythmia-specific questionnaires for patient-reported outcomes

Questionnaires and references	**SCL** [10,82-83]	**AF-QoL** [84-85]	**QLAF** [66]	**AF6** [86-87]	**PPAQ** [65]	**AFEQT** [93]
Arrhythmias developed for	Mostly AF, but used in different forms of arrhythmias	AF	AF	Persistent AF	Different forms of arrhythmias except AF	AF
Measuring symptoms?	Yes	No	Yes	Yes	Yes	Yes
Measuring HRQOL?	No	Yes	Yes	No	Yes	Yes
Scales/domains	Two scales Frequency 16 items Severity 16 items	Three domains Psychological domain 7 items Physical domain 11 items Sexual domain 3 items	Symptoms mixed with effects, treatment	6 items	Frequency, duration, symptom list with 18 items, effects 9 items, work and activities 2 items	Four domains Symptoms, daily activities, treatment concerns, treatment satisfaction 20 items
Reliability	Internal consistency (α)	Internal consistency (α)	Internal consistency (α)	Internal consistency (α)	Internal consistency (α) (KR-20)	Internal consistency (α)
Test-retest and responsiveness		Test-retest Responsive-ness	Test-test Responsive-ness	Test-retest Responsive-ness		Test-retest Responsive-ness
Validity	**Content:** expert panel	**Content:** expert panel, interviews **Construct:** EFA, convergent, Rasch,	**Content:** expert panel **Construct:** convergent	**Content:** Interviews **Construct:** convergent, discriminant, Rasch **Criterion:** "Known-groups"	**Content:** expert panel, interviews **Construct:** EFA	**Construct:** EFA, CFA, convergent**,** discriminant **Criterion:** "Known-groups"

SCL=Symptoms Checklist; Frequency and Severity Scale, AF-QoL= Atrial Fibrillation Health-Related Quality of Life questionnaire, QLAF= Quality of Life Symptom Based Atrial Fibrillation, PPAQ= Patient Perception of Arrhythmia Questionnaire, EFA =Exploratory Factor Analysis, CFA= Confirmatory Factor Analysis, α=Cronbach´s alpha coefficient, KR-20= Kuder-Richardson 20

Conceptualizing assessment of symptom burden and Health-Related Quality of Life

In the development work of a disease-specific questionnaire, such as ASTA, it can be useful to have a conceptualizing model to ensure the inclusion of relevant and necessary domains (psychological, mental and social domains). The ASTA questionnaire domains can be described in a model developed by Wilson & Cleary and further revised by Ferrans. This is a conceptual model of patient outcomes and Health-Related Quality of Life. [62,64] In the original model there

were five subsections divided in: biological and physiological variables, symptom status, functional status, general health perceptions and overall QOL. Further there was a nonmedical factor section and two overall influencing factors, characteristics of the individual and characteristics of the environment. In the revised model there were no major changes in the five subsections.[62,64]

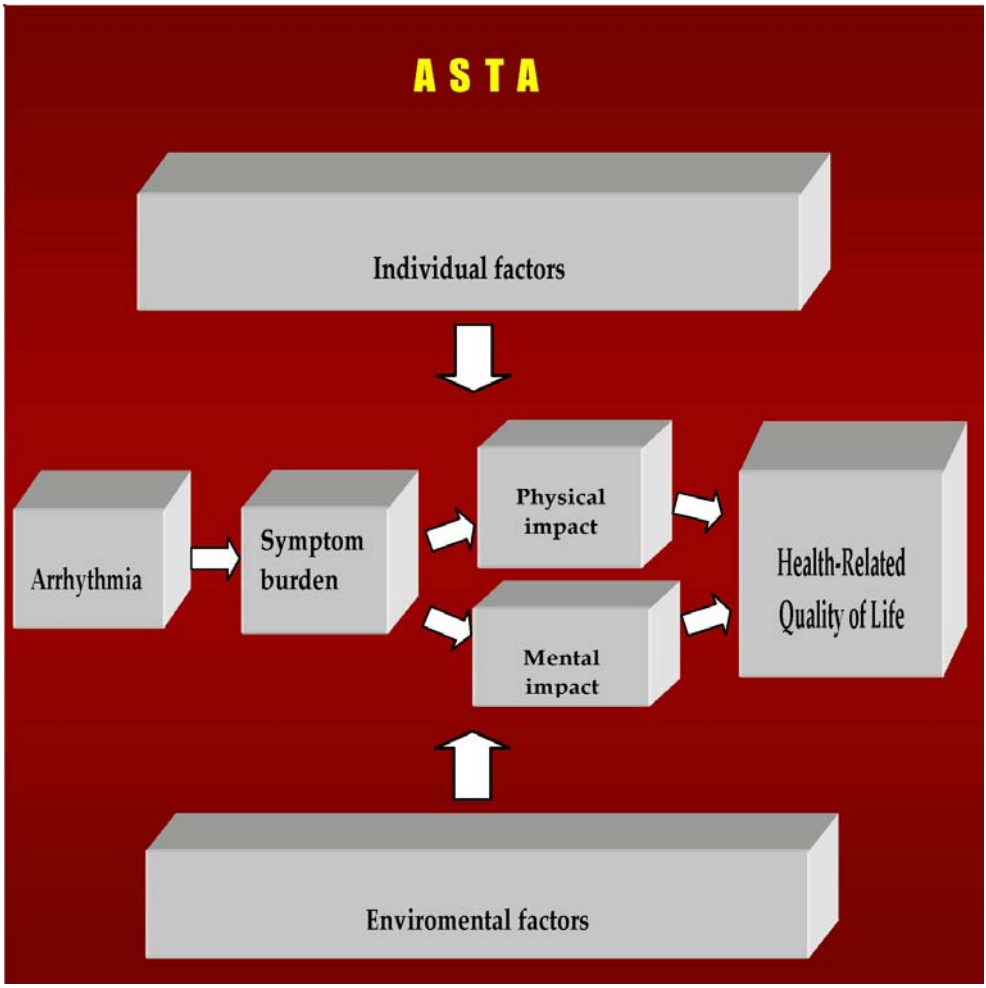
Conceptualizing symptom burden and Health-Related Quality of Life assessment in the ASTA questionnaire

The conceptualizing model for ASTA's different domains can be as described in Figure 1. The first subsection with biological (/physiological) factors can include the arrhythmia diagnosis (**arrhythmia**) by measurements of ECG, blood samples and physical assessments. The second subsection is symptoms (**symptom burden**) and can include both physical (dizziness) and mental (worry) symptoms. Subsection three is about functioning, including physical functioning with limitations in physical capacity (**physical impact**), for mental status by low spirited or sad and irritated or angry (**mental impact**) and social functioning concerning spending time with others (**mental impact**). Fourth subsection is the perception of general health, referring to all of the preceding concepts and the fifth subsection is overall QOL (**HRQOL**), assessing the patients' experiences of well-being and in the ASTA model narrowed to represent the patients**'** HRQOL. The overall individual factors are represented in ASTA by age, gender, education and daily activities (**individual factors**) and environmental factors explored by social status, i.e. if living together with someone or living alone (**environment factors**).

The arrows in Figure 1 indicate the arrhythmia's influence on the patient and the direction of the influence.

Conceptual model for the development of the disease-specific questionnaire ASTA

Figure 1



(The arrows indicate the direction of influence)

METHODS

Design and Setting

All four studies were quantitative with a cross-sectional or prospective design. Studies I and II were single-centre studies and were utilized with age and gender matched reference groups. In Study I the reference group was from the development and validation work of the Swedish translation of SF-36 and in Study II the reference group was from the same local area as the patients and with adjusted age for the twelve months follow-up. Both reference groups represented a general population.
Studies III and IV were multicentre studies including the University Hospital in Linköping and two county hospitals; County Hospital in Jönköping and County Hospital in Kalmar, Sweden. In the initial phase in Studies III and IV there were patients planned for DC-conversion at the County Hospital in Jönköping and patients at the University Hospital in Linköping planned for DC-conversion or for RFA. The DC-converted and RFA treated patients were consecutively included. In the validation part in Studies III and IV patients seeking emergency care due to AF at the two county hospitals were conveniently included and patients referred for RFA at the university hospital were consecutively included. The designs of the studies are further described in Table 2.

Table 2 Overview of Studies I-IV

	Study I	**Study II**
Aims	To describe and compare Health-Related Quality of Life in patients suffering from AV- Nodal reentry tachycardia or Wolff-Parkinson-White syndrome in patients referred for radiofrequency ablation compared to age and gender matched reference groups.	To evaluate the impact of radiofrequency ablation on Health-Related Quality of Life in patients with paroxysmal supraventricular tachycardia compared with a norm population one year after treatment.
Patients (pts) **Age and gender matched matched reference groups (**ref. group)	At baseline176 RFA pts (i.e. 97 AVNRT, 79 WPW) At 3 months 169 pts At 12 months 157 pts Baseline ref. group age and gender matched for AVNRT pts ,194 persons Baseline ref. group age and gender matched for WPW pts, 1399 persons 12 months ref. group age and gender matched for the initial PSVT pts, 176 pts, 4882 persons	
Treatment /intervention	RFA due to AVNRT or WPW	RFA due to AVNRT or WPW
Age, mean and SD	48 ±16 PSVT (all pts) 53 ±16 AVNRT pts 53 ±16 ref.group 42 ±15 WPW pts 43 ±14 WPW ref.group.	48 ±16 pts * 49 ±18 ref.group
Gender (Female/Male)	91/85 pts 130/64 AVNRT ref. group 463/936 WPW ref. group	91/85 pts 2738/2144 ref. group
Methods	Cross-sectional Questionnaires: EQ-5D, SF-36, arrhythmia-specific questions	Prospective Questionnaires: EQ-5D, SF-36,
Analyses performed	Descriptive statistics, Chi square test, Student's unpaired t-test	Descriptive statistics,, Chi square test, Student's unpaired t-test, One-way repeated measure ANOVA

Study III	**Study IV**
To develop and validate a disease-specific symptom burden scale for patients with different forms of arrhythmias i.e. supraventricular arrhythmias including atrial fibrillation and ventricular arrhythmias and to describe patient-reported arrhythmia symptoms.	To develop and validate a disease-specific questionnaire evaluating Health-Related Quality of Life in patients with different forms of arrhythmias i.e. supraventricular arrhythmias including atrial fibrillation and ventricular arrhythmias.
Initial testing Study III 534 pts 294 AF, DC-converted 96 pts and 144 RFA pts Initial testing Study IV 240 pts DC-converted 96 pts and 144 RFA pts Studies III and IV validation 270 pts 215 pts treated with RFA, 55 pts seeking emergency care due to AF No reference groups	
RFA due to most forms of arrhythmias or seeking emergency care due to AF	RFA due to most forms of arrhythmias or seeking emergency care due to AF
59 ±13pts	
93/177 pts	
Cross-sectional Questionnaires: SF-36, SCL, ASTA	Cross-sectional Questionnaires: SF-36, ASTA
Descriptive statistics, Kolmogorov-Smirnov test, Cronbach´s alpha coefficient, Pearson's and Spearman´s correlations	Descriptive statistics, Kolmogorov-Smirnov test Cronbach´s alpha coefficient, Pearson's and Spearman´s correlations Confirmatory Factor Analysis

*At baseline at the time for the inclusion. RFA= radiofrequency catheter ablation, AVNRT= AV-Nodal reentry tachycardia, WPW= Wolff-Parkinson-White syndrome, PSVT= Paroxysmal supraventricular tachycardia, AF= atrial fibrillation, DC-converted= direct current cardioversion, EQ-5D= EuroQol five dimensions and visual analogue scale, SF-36= MOS 36-item Short-Form Health Survey, SCL= Symptom Checklist; Frequency and Severity Scale and ASTA= Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia.

Participants

To fulfill inclusion criteria in the studies the patients should be ≥18 years, physically and mentally capable to fill in the questionnaires, with sufficient knowledge of the Swedish language and willing to participate. (Flow chart Figure 2)

Study I

Patients referred for RFA with the diagnosis AVNRT or WPW at the University Hospital in Linköping were asked about participation. These two patients groups were chosen because these were the two most common diagnoses at the time for Studies I and II. There were 176 patients participating referred for RFA due to WPW or AVNRT during the two year inclusion period.

Data for the age and gender matched reference groups were obtained from the working group in Gothenburg, responsible for the developmental validation work of the Swedish version of SF-36 (version1.0) within the International Quality of Life Assessment (IQOLA) Project. [72] From this work, there were data available on HRQOL representing a normative population with 8930 individuals (general population) measured by SF-36, which made it possible to match the reference groups with the patient groups according to age and gender. The comparisons between reference and patient groups in the study are comparisons in SF-36's eight scales (comparisons on group level).

Study II

The patients in Study II consisted of the AVNRT and WPW patients participating in Study I, at the time for their follow-up appointments. In the follow-up evaluation at three months follow-up, 169 patients completed the questionnaires and 157 patients at the 12 months follow-up. Two AVNRT patients had a relapse of their arrhythmia during the study period and were treated twice during the follow-up period. These patients' follow-up assessments are from the follow-up after their second RFA.

In this study the reference group participants were selected from the National Tax Population Register and included people living in the Southeastern part of Sweden, representing the same geographic area as the patient population. The reference group had completed the SF-36 and the EQ-5D index. Data on 13440 individuals, aged 18 to 84 years, were collected. From this group, 4882 individuals were selected for the present study. The reference group was selected according to the same age and gender matched distribution (comparisons on group level) as those with PSVT at the 12-month follow-up. Here it was possible to achieve data concerning concomitant diseases, for example hypertension, heart disease, diabetes, malignancy, stroke and lung diseases. [94]

Study III

Initial testing

The ASTA symptom burden part was the part first developed and has been initially tested in a total amount of 534 patients with different forms of arrhythmias. The testing started with 294 AF patient randomized to either anti-arrhythmic drugs or RFA treatment in a multicenter, international study. [95] Furthermore, 96 patients treated with DC-conversion due to AF or AFL and 144 patients referred for RFA were included. The RFA patients suffered from AVNRT, WPW, FAT, atrial macro-reentry, AFL, AF or ventricular arrhythmias (PVCs and VT).

Validation

Participants in the validation phase in Study III were represented by 270 patients, of whom 215 patients were treated with RFA and 55 patients sought emergency care due to AF. The RFA patients suffered from the same forms of arrhythmias as earlier described in the initial phase. The AF patients seeking emergency care were conveniently included and there was no data available concerning if not participating.

Study IV

Initial testing

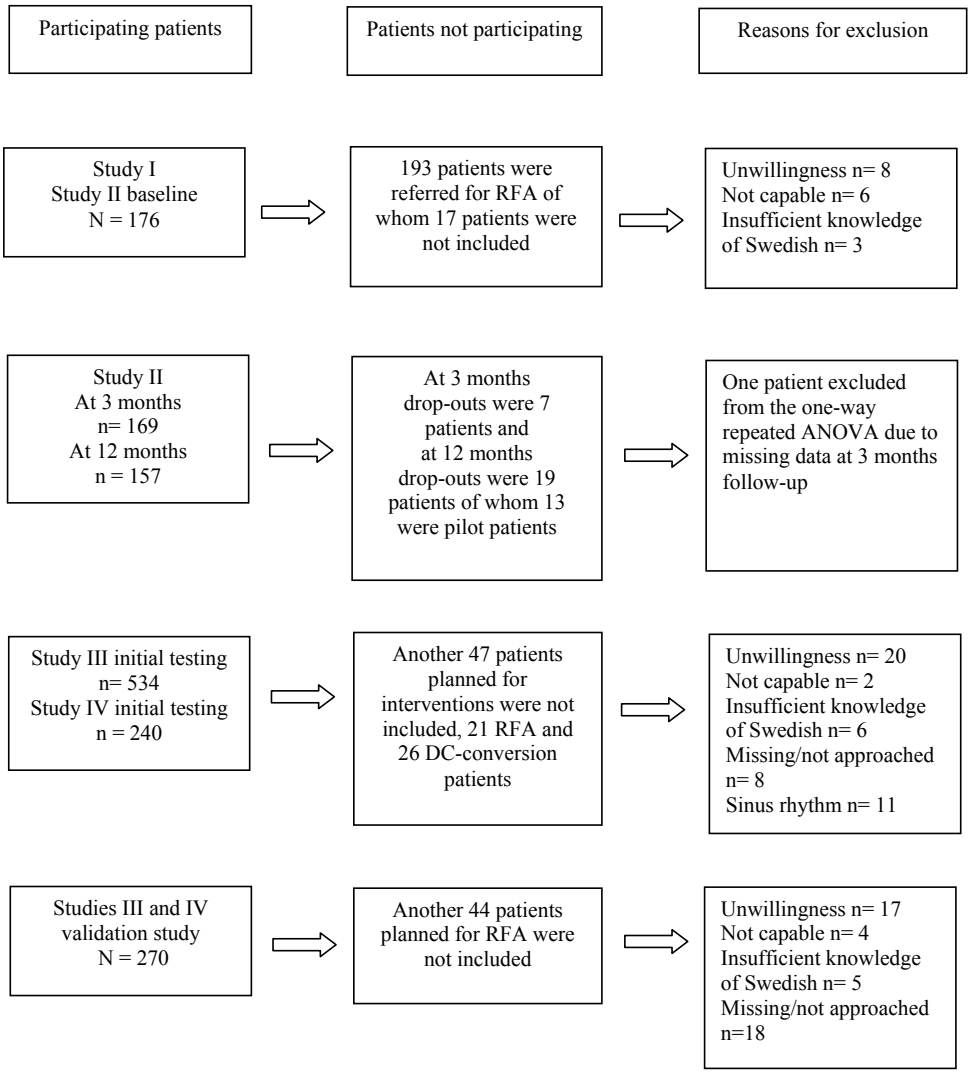
The ASTA HRQOL scale was developed during the initial testing for Study III and has therefore been tested in fewer patients (240 patients), treated with DC-conversion or RFA suffering from the same arrhythmias as the patients in the initial testing in Study III.

Validation

Participants in the validation phase in Study IV were the same patients as in Study III.

Figure 2

Flow chart of the participating patients in Studies I – IV



Data collection

Procedures

RFA patients in Studies I-IV

The RFA patients received posted study information before the intervention and got oral and written information at the time for admission to hospital, before the planned intervention. The patients were asked about participation at the time for admission to hospital. In Studies I and II they gave their written informed consent and in Studies III and IV they gave oral informed consent. The RFA patients filled out the questionnaires before the treatment and mostly the day before RFA. In Study II patients received posted follow-up questionnaires and if these were not returned within four weeks the patients were sent a reminding letter and if needed, contacted by means of a phone call.
In Study I patients were asked arrhythmia-specific questions concerning: frequency of the attacks (less than once a month compared to more than once a month) duration of the attacks (minutes compared to hours) and if they had experiences of some predefined symptoms (pronounced tiredness, shortness of breath, dizziness or anxiety) during arrhythmia and if the symptoms were experienced during activity or even at rest. Patients were questioned about concomitant diseases and when needed information was obtained from the medical records (**I**).

DC-converted patients in Studies III-IV

At the hospital in Jönköping and the hospital in Linköping the patients were approached and received written and oral study information before the planned DC-conversion. They were asked about participation on the day for the DC-conversion and gave their oral consent. The questionnaires were filled out after the ECG was taken but before the treatment, on the day planned for the DC-conversion.

AF patients seeking emergency care in Studies III-IV

Patients seeking emergency care due to AF were approached and given written information at the time for the acute care visit and gave their written informed consent. The patients received the questionnaires at the emergency visit and filled them out at the time for the visit or at home, and if so, then handed them in at a follow-up visit within two weeks after the first visit. These patients were included in the validation work of the ASTA questionnaire because the ASTA questionnaire was used for evaluations of disease-specific symptom burden and HRQOL. This separate study project included AF patients and took part at the two county hospitals. These patients did not fill out the SCL.

Questionnaires used in the studies

For the questionnaires SF-36 and EQ-5D permission was given for their use and for SCL the authors were contacted and asked for permission.

Both healthcare professionals involved in the study project and participating patients received written information about the questionnaires, including in what order to fill them out, i.e. to start with the generic SF-36. When the questionnaires were handed out the patients were encouraged to ask for help if needed.

SF-36

The well-validated SF-36 (version 1.0) was used to assess general health in all studies (I-IV). SF-36 is a generic questionnaire designed to measure an individual's physical and mental health and comprises 35 items grouped into eight scales where one question concerning changes in health is outside the scales. The eight scales represent physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health (GH), vitality (energy/fatigue (VT)), social functioning (SF), role limitations due to emotional problems (RE) and mental health (psychological distress and psychological well-being (MH)). The eight scales are summarized in two dimensions, physical

and mental component summary (PCS/MCS). For each of the eight scales and the two dimensions, scores were coded, summed and transformed to a scale from 0 (worst possible health) to 100 (best possible health). The scoring in SF-36 data was carried out as described by Ware and colleagues. [72,78,96-101] SF-36 has been widely used in research and has been demonstrated to have good psychometric properties in different populations, including patients with arrhythmias.[10-11,13,55,89,102-103]

EQ-5D

EQ-5D is a validated generic questionnaire designed to assess HRQOL's state profile. EQ-5D consists of two different types of measurement and those are the EQ-5D descriptive system and EQ VAS. The descriptive system consists of five questions exploring five different dimensions, each with three levels of severity describing patients' mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The alternative answers in each of the scales are graded and given an index according to a particular set of weights where 1.0 represents full health and -.59 represents the lowest possible index. The EQ VAS has one question assessing self-rated health status on a graduated (0-100) visual analogue scale (VAS) with 100 (best imaginable health state) and 0 (worst imaginable health state). [75-76,80,104-106] The EQ-5D has been used in many different patient populations and also in research in patients with arrhythmias. [107-108]

SCL

The SCL is a disease-specific checklist measuring arrhythmia-related symptoms and perception of the frequency and severity of the arrhythmia during the last month. SCL is mostly used in patients with atrial fibrillation but has also been used in patients with other supraventricular tachycardias treated with RFA. The SCL consists of 16 items for symptom frequency and scores from 0 to 64 (from never having the symptoms to always having the symptoms) and with 16 items for symptom severity scoring from 0 to 48 (mild to extreme). The higher the frequency score, the greater frequency with which symptoms are experienced and the higher the severity score the greater severity of the symptoms

experienced, i.e. lower scores represent better status.[10,82-83] In this thesis Cronbach's alpha was 0.88 for the frequency scale and 0.89 for the severity scale.

Development of the ASTA questionnaire

ASTA symptom burden

Development of the ASTA questionnaire started with the insight of the necessity of a suitable questionnaire for different forms of arrhythmias to evaluate patients' situation due to their arrhythmia problems. Striving at reaching a high content validity we used different methods to identify items relevant for the ASTA questionnaire. At start-up we performed a comprehensive literature review conducted in Medline to identify representative symptoms to cover the different forms of arrhythmias aimed to be included using the search terms "arrhythmia-related symptoms", "arrhythmias", "supraventricular tachycardia" and "paroxysmal supraventricular tachycardia". In addition, patients with different forms of arrhythmias referred for RFA were interviewed by the author of this thesis about their symptoms related to arrhythmia episodes and their experiences of the arrhythmia's influence on daily life situations. From this, and in combination with clinical experiences, the author responsible for this thesis created symptom questions in collaboration with a long-term experienced electrophysiologist. The eight symptom questions were thereafter evaluated by an expert panel. The expert panel consisted of cardiologists and nurses working daily with arrhythmia-patients and included the "experts themselves" i.e. arrhythmia-patients referred for RFA treatment.
Two changes were recommended by the expert panel. Firstly, there was a suggestion to an explanation for the symptom cold sweat to avoid misinterpretation from patients. There was an explanation added with the words "pale, cold and sweaty" in connection to the question. Secondly, for the symptom pressure in the chest it was suggested to add discomfort which leads to ask for "pressure/discomfort" in the chest, in combination. After this the identified and evaluated symptoms were included in the ASTA's eight question symptom burden scale.

The symptoms in the symptom burden scale were: breathlessness during activity, breathlessness even at rest, dizziness, cold sweat, pronounced tiredness, chest pain, pressure/discomfort in chest and worry/anxiety.

There were three other symptoms asked for outside the symptom burden scale. The symptoms were tiredness after having arrhythmia and experiences of near syncope and syncope. Tiredness after arrhythmia was left outside due to it not being a symptom asked for during presumed arrhythmia. The patients were asked if they had experiences of the more disabling and aggravating symptoms near syncope and syncope in connection with arrhythmia episodes. These two symptoms were important to ask for but not found relevant to be included in the symptom burden scale, where more commonly expected symptoms were incorporated.

ASTA Health-Related Quality of Life

Again a literature review was conducted in Medline searching for "Quality of Life", "Health-Related Quality of life", "arrhythmias", "supraventricular tachycardia", and "paroxysmal supraventricular tachycardia". From clinical experiences, literature reviews and information from previous patient interviews by the author of this thesis, domains were identified for questions concerning arrhythmias influence on the patients' daily life situation, i.e. HRQOL, again in collaboration with the electrophysiologist. The expert panel evaluated the newly created questions. This resulted in one more question suggested from patients and this was a question asking if the arrhythmia interfered with intimacy and sexual life. There were recommendations to improve the questionnaire with a more logical order of the questions. Thereafter questions were rearranged to be clustered in domains where they were expected to belong, i.e. in physical and mental domains. The wording "daily life" was changed to "life situation". The HRQOL questions were reworded to distinctly ask if the arrhythmia caused impairment in their HRQOL.

Development and initial testing of the ASTA questionnaire

During development and evaluation of the ASTA questionnaire patients were repeatedly encouraged to comment and suggest additional symptoms and domains if they found any missing. We tested the symptom worry/anxiety in combination and worry separately where the combination was found to be more correlated to the symptom burden scale, and therefore suggested to be combined for the revised ASTA questionnaire. Two more symptoms were added to the ASTA symptom burden scale, from suggestions from AF and AFL patients; weakness and infirmity. The expression tachycardia attacks had to be changed to heart rhythm disturbance to suit the different forms of arrhythmias the questionnaires was developed for. Concerning the HRQOL scale there was a division of one item**:** "Do you spend less time with your relatives, friends, and acquaintances (people you do not know that well) than you would like to, due to your arrhythmia?" This was divided to ask for relatives and friends in one question and for acquaintances separately due to recommendations from patients. There were some other questions asking if the patients tried to hide arrhythmia occurrence for relatives, friends and acquaintances and if the patients had experiences of been neglected while having arrhythmia. These questions were included in the initial testing but considered to be not relevant for measuring HRQOL and therefore excluded from the revised HRQOL scale. The revised HRQOL scale consisted of 13 items describing the arrhythmia's influence on daily life situation, with seven items in the physical subscale and six items in the mental subscale.

Table 3 Evaluations of reliability and validity in ASTA

	"What" **Method**	**"Why"** **Reason**
Data quality	Data distribution Missing data pattern	Scales producing scores with good data quality?
Reliability		
Internal consistency	Homogeneity among the items	Do items form a scale with internal consistency?
	Item-total correlations adjusted for overlaps	Do items form a scale with internal consistency?
Validity		
Content	Interviews, expert panel and literature review	Adequate content and domains for the targeted patients - covering relevant items?
Construct	Item-total correlations adjusted for overlaps	To what extent do the items relate to the construct?
	Convergent and discriminant validity	Evaluate to what extent the scales are correlated to other constructs
	Dimensionality	To evaluate items' expected underlying latent construct (dimensionality)
Criterion	Concurrent with "Golden standard"	Correlations between the new and an existing questionnaire?

"How" Statistic analysis	**Acceptable level**	**Study III tests performed**	**Study IV tests performed**
Descriptive statistics Kolmogorov-Smirnov test	The majority of answers not at minimum or maximum score	x	x
Cronbach's alpha (α)	$\alpha \geq 0.70$	x	x
Lower bound confidence interval for Cronbach's alpha	$\alpha \geq 0.70$	x	x
Pearson's correlations (r)	$r \geq 0.30$	x	x
Qualitatively evaluation		x	x
Pearson's correlations (r)	$r \geq 0.30$	x	x
Spearman's correlations (r_s)		x comparisons with SCL, SF-36	x comparisons with SF-36
MultiTrait MultiMethod (MTMM)			x
Confirmatory factor analysis (CFA)	non-significant χ^2 GOF and CFit, SRMR as close as 0 as possible, RMSEA ≤ 0.05, CFI and NNFI ≥ 0.95		x
Spearman's correlations (r_s)		Comparisons with SCL	

GOF= Goodness-of-fit, χ^2 =Chi square, CFit = Close fit using, SRMR= standardized root mean square residual, RMSEA= root mean square error of approximation, CFI = comparative fit index, NNFI = non-normed fit index, SCL = Symptoms Checklist; Frequency and Severity Scale, SF-36 = MOS 36-Item Short-Form Health Survey

Validation of the ASTA questionnaire's symptom burden and Health-Related Quality of Life scales

Validation of a questionnaire is a process to determine that the questionnaire measures what it is intended to measure. Validity refers to whether the questionnaire measures what it was intended to measure and reliability refers to the accuracy and consistency of the measurements.

The validation process included several steps to ensure ASTA's symptom burden and HRQOL scales properties would measure the underlying construct meant to be measured.
The quality of data was evaluated concerning distribution of answers and missing data pattern. Content validity was supplied by literature review, patient interviews and repeated expert panel evaluations.
The construct validity of the three scales in the ASTA questionnaire was evaluated with item-total correlations within respective scale, in the symptom burden scale, the total HRQOL and the physical and mental subscales.
Construct validity was further examined by convergent and discriminant validity for the ASTA symptom burden scale with correlations between the arrhythmia-specific SCL's scales and between the generic questionnaire SF-36's scales.
Concerning the HRQOL scales convergent and discriminant validity this was examined with correlations between the physical and mental scales in SF-36 (MCS, PCS) and the physical and mental subscales in ASTA.
Furthermore the construct was examined through dimensionality of the HRQOL scales tested with confirmatory factor analysis (CFA) to evaluate the model fit to the beforehand expected physical and mental subscales.
Criterion validity was possible to examine for ASTA symptom burden scale through concurrent validity to the "golden standard" arrhythmia-specific SCL.

Reliability (homogeneity)

Evaluations of the homogeneity between the items in respective scale were tested with Spearman´s correlations. Internal consistency reliability was evaluated with Cronbach´s alpha coefficient (α) for the scales.

Statistical analysis of data

The statistical analysis in this thesis was overall based on the level and the distribution of the data.

Statistical tests in Studies I and II

In the studies demographic data concerning age was described by mean and standard deviation (SD) for the patients and their reference groups and with percentage and frequencies, describing the characteristics of the sample. Comparisons for categorical variables were performed by the Chi square ($\chi 2$) test for comparisons of gender between patients and reference groups (**II**) and concomitant diseases between patients and reference groups (**II**), the frequency, duration and for the experiences of symptoms during arrhythmia episodes between AVNRT and WPW patients (**I**).

Student's unpaired *t*-test was used to compare mean scores in SF-36 and EQ-5D index and EQ VAS between AVNRT and WPW patients and in comparisons between patients and the reference groups. This included comparisons concerning the influence of age, gender, frequency, duration and symptoms during the arrhythmia attacks in the PSVT patients (AVNRT and WPW patients analyzed together) (**I**). Student's unpaired *t*-test was also used in comparisons between the PSVT group and the reference group at follow-up one year after RFA treatment (**II**). One-way repeated-measure analysis of variance (ANOVA) with Bonferroni corrected post hoc analyses were used to evaluate changes in HRQOL over time, before and after three and twelve months after treatment with RFA (**II**).

A p-value of <0.05 and 95 % confidence interval was considered significant in the studies. Data were analyzed using SPSS program for Windows (SPSS, Inc., Chicago, IL) version 14.0 (**I**) and 17.0 (**II**).

Statistical tests in Studies III and IV

In the studies descriptive statistics were used to describe demographic data and patient-reported symptoms by mean, standard deviation (SD) and frequencies. ASTA´s symptoms, symptom burden scale and 13 item HRQOL scale were psychometrically evaluated regarding data quality; construct validity and internal consistency reliability. In addition, the ASTA symptom burden scale was evaluated concerning criterion validity.
The data quality was evaluated regarding distribution of scores described by frequencies of item responses and the pattern of missing data, described with frequencies, and also with frequency of floor and ceiling effects. Floor and ceiling effects were defined if the scores (values) of the observed variables fell at minimum or maximum possible score [109], meaning if the majority of scores were distributed at either end of the response scale. The Kolmogorov-Smirnov test was used to evaluate if the scores in the symptom burden scale (**III**) and in the HRQOL scale (**IV**) deviated from a normal distribution.[110]

Construct validity was initially evaluated using item-total correlations adjusted for overlaps exploring the relation between items in the ASTA symptom burden scale and in the HRQOL scales respectively. For item-total correlations, adjusted for overlaps, the acceptable level was set to ≥0.30. [109] As a part of construct validity, convergent and discriminant validity were evaluated using Spearman's correlations. To support convergent and discriminant validity for the ASTA symptom burden scale the scale was hypothesized to correlate more strongly with SCL's frequency and severity scales compared to the scales in SF-36. Construct validity for the ASTA HRQOL scale was evaluated regarding convergent and discriminant validity using the multitrait-multimethod (MTMM) correlation matrix. [111] For this purpose Spearman's correlations between the physical and mental subscales in ASTA HRQOL and the PCS and MCS in SF-36 were examined. To support convergent validity according to the method, the strongest correlation was expected to be demonstrated between the ASTA physical scale and SF-36 PCS and between the ASTA mental scale and SF-36 MCS (homotrait-heteromethod correlations). To support discriminant validity weaker correlations should be present between the ASTA physical scale and SF-36 MCS and between the ASTA mental scale and SF-36 PCS (heterotrait-heteromethod correlations).

Confirmatory factor analyses (CFA) were used to evaluate the suggested measurement model including a physical and mental subscale in the ASTA HRQOL scale. A diagonally weighted least square estimation based on polychoric correlations and an asymptotic covariance matrix was used as the data were judged as ordinal. [112] We evaluated the goodness-of-fit between the measurement model and data by following the guiding principles described by Brown.[113] For the final improvement of model fit, the measurement error variances were allowed to correlate in a re-specified model, based on the modification index. [114] The critical N value (calculated by Lisrel software**)** suggested a sample size of at least 149 for the one factor model and 83 cases for the two factor model.

Criterion validity was established with examination of concurrent validity between the ASTA's symptom burden scale and SCL´s frequency and severity scales where SCL represented the "golden standard". A moderately strong correlation between SCL's scales and ASTA's symptom burden scale was expected to support the criterion validity, as the symptom burden scale in ASTA includes only symptoms while SCL consists of both symptoms and consequences on daily life.

Homogeneity between the symptoms in the symptom burden scale and the items in the HRQOL total scale and the physical and mental subscales were evaluated with Spearman´s correlations due to the level of data (ordinal level). The internal consistency reliability was evaluated with Cronbach´s alpha coefficient (α) in the ASTA symptom burden scale and in the ASTA HRQOL scales. [109,115] An α coefficient ≥0.70 was considered sufficient and in addition, lower bound confidence interval (95 %) for Cronbach´s alpha was calculated to ensure the lower bound to reach a level of at least ≥0.70. [109-110]

A p-value of <0.05 and 95 % confidence interval was considered significant in the studies. Data were analyzed using SPSS program for Windows (SPSS, Inc., Chicago, IL) 18.0 (**III-IV**) in study III with Stata 11.1 for Windows (Stata Corporation, College Station, TX) and study IV also with Lisrel 8.8 for Windows (SSI, Inc., Lincolnwood, IL).

Complementary statistical tests for the frame

Cohen's d effect size (ES) was used to estimate the importance of changes in HRQOL between baseline and 12 months assessments. A small ES was described as 0.2, a medium 0.5 and a large ES to 0.8.[71,116-117] Mann-Whitney U test was used for gender comparison concerning symptoms and symptom burden scale and for HRQOL items. The new results are marked with $\mathcal{F}$ before the roman number of the article in the Result and Discussion section.

ETHICAL CONSIDERATIONS

The studies comply with the Declaration of Helsinki and the guidelines of International Conference on Harmonisation in Good Clinical Practice (ICH-GCP) to protect the participating patients and to show respect for their rights and well-being.[118-119] The ICH GCP Guideline aims to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the acceptance of clinical data by the regulatory authorities.

Patients in Studies I, II and those seeking emergency care in Studies III and IV gave their written informed consent. For the initial and validation evaluations we asked for permission to obtain orally given informed consent for the DC-conversion and RFA patients. This was approved by the Regional Ethical Review Board, and the consent was documented in the patients' medical records. Patients received both oral and written study information and most patients received written study information twice before the planned intervention**,** i.e. patients planned for DC-conversion and RFA, and had time for consideration. It was only the patients seeking emergency care that did not receive written study information beforehand. Patients were informed that study participation was a choice, they had the possibility to decline to participate without any negative influence on the planned treatment and that they could whenever they wanted quit the study participation. During the follow-up period patients were contacted if the questionnaires were not returned or if there were missing data. Some were sent reminders and others contacted by a phone call but none of them were forced to fill out the follow-up assessments.

No extra interventions were performed due to the studies and therefore there were no extra risks for the patients when accepting to participate. Patients' integrity has been respected through the coded and confidentially handled questionnaires and all data are presented on a group level. And to ensure the quality of data in the data bases, the data have been checked after the imputation to see to their accuracy.

There are no obvious benefits for the patients in the study. But, a positive consequence from participation was to have an extra contact person at the

university hospital in case of late occurring questions or if experiences of relapse of the arrhythmia after treatment. Botherations for the patients were the time spent in filling out the questionnaires and for some the experiences of being asked “private questions” concerning their intimacy and sexual relations. Most patients felt encouraged and positive to share their experiences of living with arrhythmia and appreciated the possibility to describe their daily life situation and to be a part of developing a suitable “working tool” for healthcare providers.

RESULTS

Symptom burden

(F indicates result only presented in the frame)

Most patients (78 %) reported the presence of the predefined symptoms pronounced tiredness, shortness of breath, dizziness or anxiety and 49 % had experiences of the symptoms even at rest during arrhythmia. Forty-eight percent of the patients had arrhythmia durations of hours compared to minutes and 66 % had attacks more often than once a month (**I,** $\mathcal{F}$ **I**).

The patients completing the ASTA symptom burden scale reported general experiences of seven of the nine symptoms included in the scale ($\mathcal{F}$ **III**). The most commonly experienced symptoms of arrhythmia were weakness, infirmity, breathlessness during activity and pronounced tiredness and these symptoms were also the most burdensome for the patients. Tiredness after an arrhythmia attack was commonly reported (74 %) and some had experienced serious symptoms such as near syncope and syncope (32 % and 11 % respectively) in connection to the arrhythmia (**III**).

Patients were asked about how they experienced the arrhythmia, i.e. palpitations. Many felt a rapid heart rhythm and more than half experienced the arrhythmia as being irregular. The patients were asked to estimate the duration of their arrhythmia and 40 % had episodes shorter than seven hours, but 12 % had duration of more than 48 hours. Eight percent had not had any arrhythmia during the three month period before treatment. Conversely 36 % had had episodes more often than 15 occasions or experiences of arrhythmia daily. Approximately one third of the patients found the arrhythmia to appear on special occasions and 17 % mentioned food or drinks, often alcohol, to have an influence on the arrhythmia's appearance. Less than half of the patients were able to interrupt the arrhythmia by self-management (**III**). Some self-management strategies mentioned by the patients were taking "the pill in the pocket", resting or exercising and for some to drink cold water ($\mathcal{F}$ **III**).

There were differences between the AVNRT and WPW patients where AVNRT patient had longer arrhythmia attacks and more often experienced symptoms even at rest. No differences were documented concerning the frequency of the arrhythmia attacks between the groups (**I**).
Gender difference found in Study I was that female patients more often had symptoms of their arrhythmia attacks, but no differences were found concerning the duration and frequency of the attacks (♀ **I**). Analyzing the symptoms separately in the symptom burden scale we found no gender differences in how often the symptoms were experienced but women reported higher grade of intensity of both worry and tiredness afterwards (♀ **III**).

Health-Related Quality of Life

Before the treatment with RFA both AVNRT and WPW patients scored significantly lower HRQOL (SF-36) than their age and gender matched reference groups, in all scales except for bodily pain (**I**). The patients' HRQOL improved after RFA and was significantly better at three months follow-up with improvement in all scales in SF-36 and in EQ-5D (**II**). The scale bodily pain, where patients and their reference groups scored equally at baseline, showed that three months afterwards RFA patients scored significantly better HRQOL than the reference group and similarly in the other seven scales of SF-36 (♀ **II**). Between three and twelve month assessments both the improvement in bodily pain (SF-36) and EQ-5D index declined. Thus, 12 months after RFA there were significant improvements compared to baseline in all scales except for the EQ-5D index (**II**). In all the improved scales in SF-36 and in EQ VAS the effect size (ES) of the improvement 12 months after RFA reached a minimum level of 0.2 and for the scale mental health (SF-36) and for EQ VAS the ES level was 0.5 for both (♀ **II**). One year after the RFA treatment, the patients (PSVT, i.e. AVNRT and WPW together) scored an equal HRQOL compared to the reference group in the SF-36 and EQ-5D index, indicating a complete restoration of the HRQOL after RFA.

Frequent arrhythmia attacks, i.e. attacks more than once a month**,** had a pronounced negative impact on HRQOL, seen in all scales of SF-36 and in EQ-5D. Those having arrhythmia-related symptoms even at rest reported lower HRQOL in the scales general health, social functioning (SF-36) and EQ VAS,

compared to those having symptoms only during activity. Longer duration, minutes compared to hours, lowered one scale in SF-36 and this was in general health (**I**).

The patients answering all items in the ASTA HRQOL were in general negatively influenced by the arrhythmia in ten of the 13 items (ℱ **IV**). The most common interferences in patients' daily life due to the arrhythmia were represented in the physical subscale such as: reduced physical ability, deteriorated life situation, inability to work and to perform daily activities and to avoid planning for things, for instance travelling or leisure activities (ℱ **IV**).

There were differences seen between the patient groups in Study I where AVNRT reported lower HRQOL than the WPW patients in the scales bodily pain, general health and physical functioning in SF-36 and in EQ VAS. Older age had a negative influence on HRQOL where patients ≥50 years scored lower in all scales of SF-36 except for vitality, and lower in EQ VAS (**I**).

Concerning differences between gender**,** women scored lower HRQOL in physical functioning, vitality and mental health and in the EQ-5D index than men did (**I**). There were gender differences found in the comparisons one year after RFA, where women scored lower HRQOL in physical functioning, vitality, role-emotional, mental health and mental component summary (SF-36) and in the EQ-5D index (ℱ **II**). When the items in the HRQOL scale were analyzed one by one concerning gender differences there were two significant differences detected. Men were more often affected with regard to the arrhythmia's interference with their sex life and they experienced reduced physical ability more often than women. Men also reported a higher grade of intensity of these problems. Conversely, women scored lower in physical functioning, mental health and mental component summary (SF-36) than men did (ℱ **IV)**.

The ASTA questionnaire

The ASTA questionnaire consists of three separate parts where part I describe demographic data, part II arrhythmia-specific symptom burden and part III HRQOL (Appendix 1).

Data quality

Of the 270 participating patients in Studies III and IV, 230 filled out all items in the symptom burden scale (**III**) and 237 the HRQOL scale (**IV**). Twenty patients had missing data for all of the items in the symptom burden scale and 19 patients for all items in the HRQOL scale. Two patients had eight, respective nine, missing values in the symptom burden scale and 18 had missing values for one to three items (**III**). In the HRQOL 13 items scale 14 patients had missing values for one to seven items. The missing data were equally distributed across both the symptom burden scale and the HRQOL scales.

The distribution of the item scores in the symptom burden scale (10 and 9 items scales) showed a floor effect for two symptoms and for four items in the HRQOL scale, none of the items showed a ceiling effect in the scales. One of the four scales deviated significantly from a normal distribution and that was the mental HRQOL subscale.

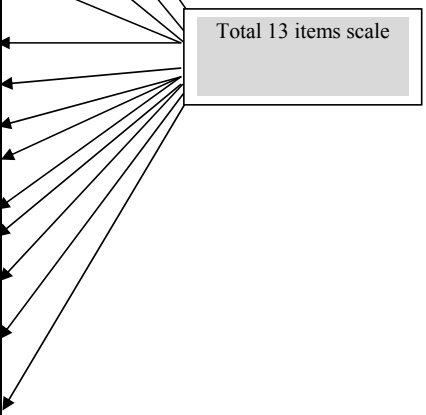
Validity

Evaluations of construct validity demonstrated that all of the nine items in the revised symptom burden scale reached the expected level of item-total correlations, above 0.3, and the same holds for the items in the HRQOL scales. This indicates that the items in each respective scale measure the same concept. Construct validity, evaluated with convergent and discriminant validity, was demonstrated for the ASTA symptom burden scale with stronger correlations with the disease-specific SCL's frequency and severity scales than with the scales of SF-36 (**III**). Convergent validity was confirmed for the ASTA's two HRQOL subscales and SF-36's PCS and MCS dimensions with the strongest correlations between physical subscale of ASTA and PCS and for the mental subscale of ASTA and MCS (**IV**). Discriminant validity was supported with lower correlations between ASTA´s physical scale and SF-36 MCS and between ASTA´s mental scale and SF-36 PCS. The strongest correlation found was between ASTA´s physical and mental subscales, not supporting discriminant validity.
Construct validity was further evaluated using the confirmatory factor analysis (CFA) to verify the beforehand hypothesized subscales in the HRQOL scale

(**IV**). The factor loading was >0.5 in the one factor model (i.e. 13 items total scale) and >0.6 in the two factor subscale model (i.e. the physical and mental subscales). The model fit was unsatisfactory for the initial one and two factor models, according to Chi square goodness-of-fit and RMSEA. In the re-specified models**,** where error variances were allowed to correlate, the model fit increased significantly for all factor models. It was now only the Chi square goodness-of-fit for the one factor model that had not reached the criteria for model fit.

Figure 3
Factor loadings for the initial 13 items one factor HRQOL model

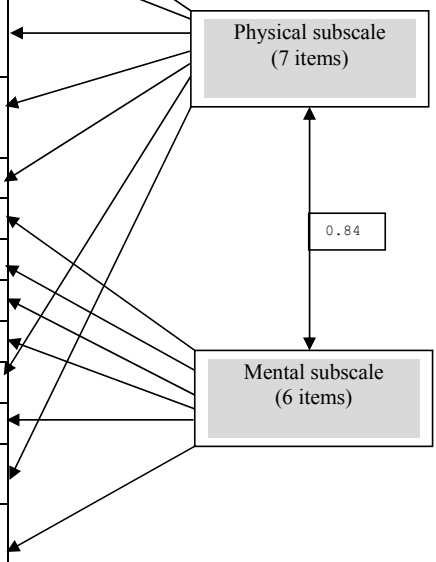
Error variance	ASTA HRQOL 13 questions (initial model)	Factor loadings
0.34	1) Do you feel unable to work, study or carry out daily activities as you would like to due to your arrhythmia?	0.81
0.20	2) Do you spend less time with your relatives and friends than you would like to due to your arrhythmia?	0.90
0.25	3) Do you spend less time with acquaintances (people you do not know that well) than you would like to due to your arrhythmia?	0.86
0.35	4) Do you avoid planning things you would like to do, for instance travelling or leisure activities due to your arrhythmia?	0.81
0.40	5) Is your physical ability reduced due to your arrhythmia?	0.78
0.36	6) Is your ability to concentrate reduced due to your arrhythmia?	0.80
0.45	7) Do you feel low-spirited or sad due to your arrhythmia?	0.74
0.61	8) Do you feel irritated or angry due to your arrhythmia?	0.62
0.66	9) Do you suffer from sleep problems due to your arrhythmia?	0.58
0.54	10) Is your sexual life affected negatively by your arrhythmia?	0.68
0.67	11) Are you afraid of dying due to your arrhythmia?	0.57
0.27	12) Has your life situation deteriorated due to your arrhythmia?	0.85
0.64	13) Do you feel worried that your symptoms will re-occur during the periods when you do not suffer from arrhythmia?	0.59



Chi square =181.55, df=65, P-value<0.001, RMSEA=0.111
(before error variance correlations)

Figure 4
Factor loadings for the initial seven items physical and six items mental subscales in the two factor HRQOL model

Error variance	ASTA HRQOL 13 questions (initial model)	Factor loadings
0.32	1) Do you feel unable to work, study or carry out daily activities as you would like to due to your arrhythmia?	0.83
0.18	2) Do you spend less time with your relatives and friends than you would like to due to your arrhythmia?	0.91
0.23	3) Do you spend less time with acquaintances (people you do not know that well) than you would like to due to your arrhythmia?	0.88
0.33	4) Do you avoid planning things you would like to do, for instance travelling or leisure activities due to your arrhythmia?	0.82
0.38	5) Is your physical ability reduced due to your arrhythmia?	0.79
0.22	6) Is your ability to concentrate reduced due to your arrhythmia?	0.88
0.33	7) Do you feel low-spirited or sad due to your arrhythmia?	0.82
0.56	8) Do you feel irritated or angry due to your arrhythmia?	0.66
0.62	9) Do you suffer from sleep problems due to your arrhythmia?	0.62
0.53	10) Is your sexual life affected negatively by your arrhythmia?	0.69
0.62	11) Are you afraid of dying due to your arrhythmia?	0.62
0.26	12) Has your life situation deteriorated due to your arrhythmia?	0.86
0.60	13) Do you feel worried that your symptoms will re-occur during the periods when you do not suffer from arrhythmia?	0.63



Chi square =167.92, df=64, P-value <0.001, RMSEA=0.105
(before error variance correlations)

Criterion validity for the ASTA symptom burden scale was demonstrated with significant correlations between the ASTA symptom burden scale and SCL's frequency (r_s =0.62) and severity (r_s =0.61) scales. There was a strong correlation (r_s>0.9) seen between the two scales within SCL (**III**).

Reliability (homogeneity)

The homogeneity between the ten items in the ASTA symptom burden scale was reflected by significant correlations between most of the items, except for the symptoms worry and breathlessness during activity, infirmity and chest pain and lastly, infirmity and pressure/ discomfort in chest. The strong correlation between the symptoms weakness and infirmity led to a revised symptom burden scale containing of nine items, where the two symptoms were combined in one item, i.e. weakness/infirmity. There was a strong correlation between a symptom outside and one inside the ASTA symptom burden scale, tiredness afterwards and pronounced tiredness during arrhythmia.

The internal consistency, demonstrated with Cronbach's α, was satisfactory for the revised nine item symptom burden scale with α 0.80, for the 13 item HRQOL scale α was 0.91, physical subscale α 0.89 and α 0.79 for the mental subscale (**III-IV**). Also the lower bound confidence interval was at a sufficient level (α>0.7) for all scales in the ASTA questionnaire. The two added symptoms weakness and infirmity were highly correlated and therefore combined to one question in the revised symptom burden scale.

DISCUSSION

The main findings were the pronounced impairment of HRQOL found in patients in comparisons to the age and gender matched reference groups. At one year after RFA patients' HRQOL was markedly improved and equal to the matched reference group. The newly validated ASTA questionnaire, assessing symptom burden and HRQOL, was found to have satisfactory psychometric properties when tested in a patient population representing most forms of arrhythmias.

Symptom burden

Most patients were symptomatic and approximately half of the patients had perceived symptoms even at rest during arrhythmia. There were also patients who did not report presence of the predefined symptoms, some due to lack of them while others could have hesitated to answers "yes" because the four symptoms were clustered into one question (**I**). Another reasonable explanation for no symptoms was the more frequent use of anti-arrhythmic therapy at the time for Study I.
The patients had experienced most of the ingoing symptoms in the ASTA symptom burden scale (*F* **III**) and tiredness after the arrhythmia was common (**III**). The chosen symptoms in the ASTA symptom burden scale are represented in most of the other symptom scales for arrhythmia-patients; in bedside scales for clinicians' use, the EHRA classification and in questionnaires for PROs. [10,33,65-66,87-88,93]

The symptom burden varies but for many arrhythmia-patients the onset is distinct and associated with symptoms ranging all from mild palpitations to experiences of nearly handicapping symptoms. [2-3,6-7,13,33] Also the symptoms near syncope and syncope were experienced by patients, confirming the importance to evaluate these disabling symptoms (**III**). Even though these distressful symptoms are more rarely present they are important to evaluate in order to capture the symptom burden in arrhythmia-patients. [3,6-7,17]

The patients were asked not only if they had experiences of the arrhythmia, but also how they experienced the arrhythmia, i.e. palpitations, for example if the arrhythmia was rapid, irregular or with a feeling of missing beats. We asked how frequent the arrhythmia occasions where and also for an estimation of the duration. With knowledge from earlier studies and from Study I frequent recurrences of symptomatic arrhythmia were known to be of great importance for the patients. [10,120] Approximately one third of the patients felt that their arrhythmia appeared at special occasions where both physical and mental factors were mentioned as well as food and special drinks being judged to influence the onset. In a study where AF patients were interviewed, similar arrhythmia-provoking factors were described: for example alcohol, coffee or to eat fatty, spicy food or eating too much, the same as mentioned by patients in Study III. [121-122] More than half of the patients were unable to interrupt the arrhythmia after the onset. This may cause troublesome effects for patients, especially for those needing acute healthcare assistance to stop the arrhythmia attack (**III**).

AVNRT patients were more symptomatic with longer duration of the arrhythmia attacks and had more often symptoms even at rest (**I**). Some differences could probably be addressed to the age and gender matched differences between the groups. Gender differences in AVNRT patients have also been documented, with female patients having higher heart rate during their arrhythmia than men.[31] It is shown that female arrhythmia-patients commonly report more symptoms and a higher grade of symptom severity than men.[6,11,13,123-124] Women had more often symptoms during their arrhythmia and more often experienced worry during their arrhythmia occasions ($\mathcal{F}$ **I**, $\mathcal{F}$ **III**). The differences confirmed earlier study findings.

Health-Related Quality of Life

The arrhythmias' negative effect on patients' HRQOL was demonstrated with the generic questionnaires SF-36 and EQ-5D and the ASTA HRQOL scale. There was a pronounced impaired HRQOL shown in the AVNRT and WPW patients (**I- II**) compared to the age and gender matched reference groups. The two patient groups had the opposite age and gender matched distribution but followed the same pattern, scoring lower in the same scales compared to their respective reference group. The treatment with RFA restored patients' HRQOL,

thus, one year after RFA the patients scored HRQOL to a similar level as the reference group (**II**). The positive effects remained during the follow-up period but with the most pronounced effects seen at the first follow-up, three months after RFA (**II**). We found it important to have age and gender matched reference groups to be representative for the AVNRT and WPW patient groups. To our knowledge, these are the first studies performing comparisons with matched normative population groups and with comparisons both before and after RFA. Even if the reference groups were matched and the questionnaires were general the patients scored significantly lower HRQOL in several domains. In other studies when arrhythmia-patients have been compared with a normative population or patients suffering from other heart diseases, arrhythmia-patients were found to score lower HRQOL.[10,13]

Longer duration and symptoms even at rest had a negative impact on HRQOL but not to the same large extent as frequent attacks had (**I**). The negative influence of frequent arrhythmia events and increased symptom severity has been demonstrated earlier.[10] The daily life situation can be unpredictable and insecure, especially for those with recurrent and frequent attacks, never knowing when the next arrhythmia occurrence will be. It can bring difficulties to find a sufficient level of pharmacological treatment, sufficient both with and without the presence of arrhythmia.[13] Arrhythmia disability with short-time absences from work or sick-leave can lead to negative consequences and costs for working-active patients. [15-16,33] In a report from a radiofrequency (RFA) centre the situation for arrhythmia-patients was described. During the time waiting for treatment patients reported worsening of the arrhythmia and working-active patients were on sick-leave due to their arrhythmia.[15] There are patients with feelings of incapacity and frustration, some reluctant to plan leisure activities and for others it can lead to self-imposed restrictions in usual activities, for example driving. [6,9,17]

Patients with SVT and AF have described problems to obtain the right diagnose and how they tried to find strategies to manage the arrhythmia, and for some this became the focus in their lives. Further, they developed strategies to appear as normal as possible and felt frustrated in their attempts to find causative factors to reduce the risk of arrhythmia recurrences. It was also shown that the patients felt emotional distress and missed support for coping with that.[8-9,125-126] In HRQOL assessment the influence of personality can play a role as well as

illness management styles and the presence of depression and anxiety symptoms have been reported in arrhythmia-patients. [14,124,127]

AVNRT patients scored lower HRQOL than WPW patients in the physical scales (**I**). Some contributing factors to this can be that the AVNRT group consisted of more female patients who were older, had more concomitant diseases and were more frequently treated with anti-arrhythmic drugs. Medication can cause side-effects and older age, female gender and other diseases can influence the level of HRQOL.[6,10,72,123-124]

When we compared women and men in the studies (**I-II,IV** and *F* **II,** *F* **IV**) HRQOL assessment showed lower HRQOL for female patients both for physical as well as for mental domains in SF-36's scales and lower in EQ-5D index. Gender differences are known from other arrhythmia studies and from general population evaluations where women usually score lower HRQOL, mostly in physical domains but also in mental domains.[72,123-124,128] Gender differences shown in other studies are that female patients have more difficulties to be believed, to achieve the correct diagnose and were treated with ablation later than men were. [9] Also symptoms of depression and anxiety are more frequently reported in women with arrhythmias. [13,123-124] In Study (*F)* IV we found gender differences in the scoring in ASTA HRQOL's scale where men reported more interference in their sexual life and experienced more reduced physical ability. The mean age in the study was relatively high and many of the male patients were suffering from either atrial fibrillation (AF) or atrial flutter (AFL). Both age and medication can cause interference in the sexual life in this patient group.

Treatment with RFA has been extensively developed for arrhythmia-patients during the last decades and with upgraded guidelines this is first line treatment for many patients. [1-2,4-5] In comparisons between RFA and anti-arrhythmic drugs, treatment with RFA shows favourable data where our data confirm the significant treatment effects after RFA. [10-11,18,103,129]

There are patients judged to be curatively treated with RFA, reporting arrhythmia-related symptoms at the time for follow-up. These findings explore the importance to evaluate our patients over time to ensure the efficacy of the performed intervention. Assessment of solely objective parameters, i.e**.**, only

ECG-measurement, is not sufficient to evaluate patients' well-being and daily life situation. The question is: What are we actually treating – our patients or their ECG's? [28,130] Assessment of PROs gives valuable information about patients' self-experienced daily life situation and can be requested from healthcare providers, authorities, pharmaceutical companies as well as from patients themselves. [24-25,27,68]

The ASTA questionnaire

Data quality

The overall data quality was satisfactory. The users' instructions were a bit vague for less symptomatic patients, therefore some did not complete all parts of the ASTA questionnaire. There were no indications of missing data pattern, indicating items to be too difficult to respond to. The instructions have now been rewritten to more clearly guide the patients on how to fill out ASTA. We have strived to achieve scales with good sensitivity and include symptoms and domains relevant for arrhythmia-patients. Even if many symptoms and daily life situations can be similarly affected it is challenging to cover relevant items for the targeted population.

The symptom burden scale was extended due to recommendations from the experts, i.e., the patients. However, the two symptoms weakness and infirmity were found to be too similar, probably measuring the same construct (i.e. redundancy). This led to a combination of these symptoms in the revised symptom burden scale after discussions in the expert panel. Tiredness after arrhythmia was known to be present in arrhythmia-patients and was therefore included in the initial and validation assessments. This symptom has also been evaluated in other work on developing a questionnaire and excluded through the validation process.[85] For the revised ASTA questionnaire we considered that tiredness afterwards should be excluded since no other symptoms were asked for after the arrhythmia was interrupted. It is important to cover relevant symptoms and domains to find valuable information without making a questionnaire too lengthy.

Data skewness was a minor problem even though some symptoms in the symptom burden scale and some items in the HRQOL scales showed floor effects. The potential risk with skewed data can be low sensitivity i.e., difficulties to discriminate between healthier and more affected patients. This can lead to a reduced ability to assess when a patient improves or deteriorates consequently influencing the ability to discriminate within and between groups. [71,109] The mental subscale in the ASTA HRQOL scale deviated from a normal distribution but the scoring range was found to be good. Even if some items showed floor effect the overall distribution of the scores was good, indicating the scales having the ability to discriminate between patients with high or low symptom burden and with more or less affected HRQOL.

From patients' recommendations we added the option to answer "I don't know" in the HRQOL scale and for the symptom tiredness afterwards, outside the symptom burden scale. Unfortunately, rather many patients had chosen this alternative. Those patients were probably less affected during arrhythmia or more doubtful if it was the arrhythmia per se that caused the negative effects. The " I don't know" option was most frequently used for the question concerning the arrhythmia's interference with the sex life. A reason for choosing this option could have been that some patients lived alone without a partner. "I don't know" was found to be difficult to interpret and has therefore been deleted in the revised ASTA questionnaire. At the same time the answer "No" was altered from "No, not at all" to just "No". The user's instructions have been rewritten and hopefully patients will find it inherent to fill out even if the "I don't know" alternative is excluded. The symptom pronounced tiredness during arrhythmia was reworded in the revised symptom burden scale to now asking for only tiredness. In the response alternatives the grade of severity was already captured, i.e. if it was pronounced or not.

Validity

All of the scales in the ASTA questionnaire were generally found to have good validity. Strengths with the study were the large amount of patients in the initial testing and validation study. The repeated evaluations in the expert panel, including patients, enable the content validity to be covered with items and domains relevant for patients with different arrhythmias. Many patients felt

encouraged to comment and make suggestions for improvement of the ASTA questionnaire. They were frequently approached and asked for opinions and were recommended to add comments in the questionnaire. The healthcare providers involved in the study project worked daily with arrhythmia-patients and most of them had long term experiences of it.

The evaluations of the construct with convergent and discriminant validity for the scales in ASTA behaved as expected. The ASTA symptom burden scale correlated stronger with the disease-specific SCL and weaker to the generic SF-36. Supporting the construct in the ASTA HRQOL scale, the physical and mental subscales correlated more strongly respectively more weakly to the expected SF-36´s PCS and MCS. We found one correlation not supporting discriminant validity and this was the strong correlation seen between the two HRQOL subscales in ASTA. Not surprising though, since items in these scales can be influenced both physically and mentally, for example by sleep disturbances and intimacy concerns. The strongest correlation found was the correlation between the two scales in SCL (r_s>0.90) indicating these two scales measuring almost the same concept. In the item-total correlations we could confirm satisfactory correlations for all of the ingoing items in respective scales, indicating them to measure the same concept.

During the development of ASTA's HRQOL scale we have strived to cover representative domains covering physical and mental aspects. Those dimensions are of importance in definitions of HRQOL and represented in other questionnaires, such as in the generic SF-36, in the disease-specific Minnesota Living with Heart Failure questionnaire and also in a questionnaire for AF patients, AF-QoL. [72,84-85,99,131] Factor analysis and Rasch analysis are common methods to evaluate construct validity. Although exploratory factor analysis (EFA) is commonly used to explore dimensionality in newly constructed scales, we have chosen to use a CFA to confirm the expected physical and mental domains.[65,85,87,93,109] With a CFA the hypothesized model can be tested for significance and data concerning error variance can be presented, something not possible in an EFA. From the literature review and clinical experiences the ingoing items were presumed to be represented within the selected domains. The item's multi-dimensionality was confirmed in the CFA, showing an increased model fit especially in the subscales. Further, with re-specified models it was

now only the one factor model that did not reach the criterion for model fit within the Chi square goodness-of-fit analysis.

Criterion validity was only possible to establish for the ASTA symptom burden scale with concurrent validity against the "golden standard" SCL. [10,82-83] The symptom burden scale correlated stronger to SCL than to SF-36 but not extremely highly. A reasonable explanation can be that SCL also includes some items exploring the consequences of arrhythmia and further some general and not arrhythmia-specific symptoms.[92] Even though examinations of construct and criterion validity for SCL have been planned, described in the user's instructions, clearly statements about validity are difficult to find. There were no possibilities given to evaluate criterion validity for the HRQOL scales because there was no disease-specific questionnaire available representing "golden standard" at the time for the validation study.

Reliability (homogeneity)

Homogeneity in the ASTA symptom burden scale was demonstrated by the correlations between most of the included items, and the internal consistency was overall satisfactory in all of the ASTA questionnaire scales. Internal consistency is often used in scales to examine the reliability. All scales reached the expected level of Cronbach's alpha (α) and the lower bound confidence interval confirmed that no data were falling under the critical level. [109-110,115] Moreover, in the α analysis the estimation of item-total correlations showed satisfactory data for all of ASTAs scales.

In the user recommendations for evaluation of measurements with SCL, the authors proposed to analyze Cronbach's α. We examined the internal consistency reliability for the two scales in SCL and both showed satisfactory internal consistency with satisfactory α values. One can expect the level of Cronbach's α to be sufficient due to the rather high number of items in SCLs two scales. A high number of items usually increase the level of α even when item correlations are modest.[71,117]

Arrhythmia-specific questionnaires for PROs assessing symptom burden and Health-Related Quality of Life

In the literature there are distinctions described between different items and between different scales. Symptom scales are described to represent clinimetric scales with causal indicators and clinical indices while psychometric scales contain effect indicators reflecting the level of QOL and HRQOL. The distinction is not always clear and some items may be both causal and effect indicators in nature and scales can have attributes of both clinimetric and psychometric scales. [61,71,132] The necessity of a distinction is also discussed where some find it just limiting and causing confusion.[133]
One symptom included in ASTAs symptom burden scale is described to be both a causal and an effect indicator and this is the symptom anxiety. It is often evaluated in arrhythmia-patients and then, mostly as an arrhythmia-specific symptom. [9,33,66,87] Our attempt has been to construct scales with assessments of symptoms and effects of arrhythmia, i.e. HRQOL separately, covering relevant arrhythmia-specific items and domains, without making it too burdensome to fill out. We have been aware of the importance of combining evaluations of both clinical relevance and psychometric properties for the scales in the ASTA questionnaire.

The construct of questionnaires varies with more or less separated sections for symptoms (causal indicators) and the consequences on patients' daily life situation (effect indicators). When we started the development of the ASTA questionnaire the disease-specific questionnaire often used for PROs was the SCL. [10,82-83] This checklist also includes items exploring the effects from arrhythmia, for example trouble to concentrate, difficulties to sleep and nonspecific symptoms like headache and poor appetite.[92]

A new, validated questionnaire, developed for supraventricular tachycardia (SVT) excluding AF patients, evaluates concerns of sleep both in the symptom section and in the section for the arrhythmia's effects on daily activities.[65] There is a short symptom rating scale for AF patients scheduled for DC-conversion where one of the items included in the symptom scale asks for effects on daily life concerns i.e. HRQOL. [86-87] Another questionnaire, described to be a quality of life questionnaire, evaluates "quality of life symptoms" in AF patients mixing symptoms and effects on daily life. [66] Except for the questionnaire developed for

SVT patients most of the recent questionnaires are solely aimed at AF patients. There is a HRQOL questionnaire for AF patients where the underlying construct is expressed in a physical and mental scale, with the similar construct as in the ASTA HRQOL scale. This questionnaire solely expresses the arrhythmia's effects on daily life, no symptoms included. [84-85] The most recently validated questionnaire is a Quality of Life questionnaire for AF patients, assessing symptoms, daily life activities, treatment concerns and treatment satisfaction.[93] The reasons for separating the symptom burden and HRQOL scales in the ASTA questionnaire were to make it possible to use the scales separately and make it more relevant for the scoring. Within the validation work with ASTA we have produced a suggestion for the scoring of the different scales in the ASTA questionnaire. (Appendix 1)

Methodological issues and limitations in Studies I-IV

There were no missing data in either SF-36 or EQ-5D in Studies I and II. It was important to encourage the patients to fill out the questionnaires before the intervention to avoid influencing (bias) the responses. If the treatment was successful or not or experienced to be painful, we thought might affect how the patients responded. All questionnaires were thoroughly checked when handed in and if there were answers missing the patients were approached and given the chance to complete. In Studies I and II 13 of the participating patients were pilot patients and therefore only planned for baseline and three months follow-up, consequently with a lack of data for these patients at 12 months follow-up.

Unfortunately, it was not possible to achieve data in Study I concerning the reference groups' concomitant diseases and if they were on medication. At follow-up we did not ask for the use of anti-arrhythmic medication after the RFA treatment (II) which would have been of interest. The anti-arrhythmic medication before the RFA could have contributed to lower the patients HRQOL.

At the time for Studies I and II there was no validated questionnaire available for arrhythmia-patients in Sweden. This could have given us a deeper understanding of the patients' situation and revealed the disease-specific

negative effects from living with arrhythmia. We asked the patients some arrhythmia-specific questions in Study I. These were clustered and probably caused some missing data when having experiences of one or some, but feeling reluctant to answer yes to all of them. We asked the patients if they had experienced near syncope and syncope at any arrhythmia occasion but we did not ask them to estimate how often this had been present.

In Studies III and IV we made some changes in the ASTA questionnaire which led to difficulties to include the first versions of ASTA data in the validation part. We have therefore described the findings from the initial testing separately. It would have been an advantage with more patients in the final validation part and we are sorry for the large amount of patients not possible to include. First we did not specifically use the search term "ventricular arrhythmias" but later we found similar symptoms described as for patients with other arrhythmia diagnoses.

The studies in this thesis have a cross-sectional or prospective design. This is a strength in comparison to studies where the symptoms have been retrospectively collected from the patient's medical records. In these reviews there is a risk for underestimation of symptoms with lack of information when patients are not approached personally. Retrospectively collected data can be dependent of the recall period, a painful intervention and if the treatment outcome was successful or not. A long recall time can bias data as well, as when within a short time period after a treatment patients can be more symptomatic as an effect from the treatment or from recently changed medication. [129,134]

The questions answered with "I don't know" in the validation work of ASTA are treated as missing data. The difficulties to interpret the answer "I don´t know" reduced the number of patients to fall just under the recommended limit for CFA, thus of the recommended 149 persons for the one factor model 147 persons were available with complete data. However, the targeted patient groups were all represented but there were too few in some groups to evaluate "known-groups" validity between different arrhythmia groups. In the correlation analysis we used pairwise deletion when possible because this enables evaluations of all the given responses, where conversely, listwise deletion excludes a patient from further evaluation if one answer is missing.

In the validation study there were AF patients seeking emergency care included in our evaluations due to the ASTA questionnaire being used for disease-specific assessments. These patients were participating in another study and therefore they had not filled out the disease-specific SCL. Therefore they were excluded from the correlation analysis between ASTA and SCL.

To develop a questionnaire suitable for most forms of arrhythmias can be challenging. Different arrhythmia can be present with a more or less pronounced symptom burden and the interference with the patients' life situation depending of the form of arrhythmia, i.e. if it appears in recurrent attacks or is present as persistent. Therefore, the initial wording where we asked for arrhythmia "attacks" had to be changed to be representative also for those with sustained arrhythmias. There are advantages with one questionnaire including most arrhythmia forms. It makes it easier to compare groups of arrhythmia-patients and then it is not necessary to know the definite diagnose at the time for filling it out. There are patients where diagnose is unknown before the RFA treatment, with patients achieving the correct diagnose during the intervention.

It has to be mentioned that studies assessing symptom burden and HRQOL in arrhythmia-patients probably contain patients more symptomatic and negatively affected of their arrhythmia and therefore seeking healthcare assistance. To keep in mind is that there are patients living with arrhythmia, without suffering from it.

CONCLUSION

Results from this thesis described how negatively affected arrhythmia-patients can be with a pronounced symptom burden and impaired HRQOL despite being relatively young and otherwise healthy. In comparisons with age and gender matched norm population patients scored significantly worse HRQOL. Some contributing factors to low HRQOL were female gender, older age and more frequent arrhythmia attacks.

Treatment with RFA is a first line therapy for many of the arrhythmia-patients and one year after treatment the patients scored an equal HRQOL compared to the norm population. This elucidates the importance to offer RFA treatment to patients with arrhythmias within a reasonable period of time.

Assessment of a patient's symptom burden and HRQOL is essential to explore the severity of a disease and to evaluate therapeutic efficacy and can be the main treatment outcome both in clinical and research settings. PROs are important to take into consideration in the care of arrhythmia-patients and cannot be replaced solely by objective measurements. Trustworthy assessments of disease-specific PROs require questionnaires developed for and validated in the targeted patient population.

The psychometric properties in the new arrhythmia-specific questionnaire ASTA were found to be overall good both for the symptom burden scale and the HRQOL scales.
To the best of our knowledge ASTA is the first arrhythmia-specific questionnaire assessing symptom burden and HRQOL, suitable for most of the different arrhythmia forms. Thereby, the newly validated ASTA questionnaire can be an important contribution to assessment of PROs in arrhythmia-patients.

CLINICAL IMPLICATIONS

A – ASTA an arrhythmia-specific questionnaire now validated and available for assessment of symptom burden and Health-Related Quality of Life, suitable for most forms of arrhythmias

S – Self-reported subjective experiences from arrhythmia-patients are of great importance, before, during and after different interventions, and cannot be replaced solely by objective assessments

T– Treatment alternatives for arrhythmia-patients depend on the form of arrhythmia, where RFA nowadays can be suitable for many. To obtain trustworthy PROs exploring treatment efficacy, questionnaires validated in the targeted patient population are required

A – ASTA questionnaire, is now in clinical use in arrhythmia-patients treated with RFA at the Dept. of Cardiology, University Hospital Linköping, Sweden, with assessment before and at follow-up after RFA and included in research projects for arrhythmia-specific assessments

FUTURE

The ASTA questionnaire needs to be further tested concerning stability (test-retest reliability) and responsiveness properties. Data collection will start in November 2011 to establish the final evaluations during 2012.

It is important to work towards the implementation of the ASTA questionnaire as a working tool in assessment of symptom burden and Health-Related Quality of Life in other healthcare institutions, clinics, interested in assessment of PROs before and after different forms of interventions.

Further, with the knowledge from this thesis an Internet-based educational program for arrhythmia-patients (especially patients suffering from atrial fibrillation) can be developed, including a cognitive behavioral therapy approach. The aims of the program would be to increase patients' knowledge about disease-specific arrhythmia concerns, improve patients' possibilities to perform self care, decrease the arrhythmia burden, and ease patients' worry/anxiety concerning arrhythmia and to improve their HRQOL.

SVENSK SAMMANFATTNING

Att leva med hjärtrytmrubbning kan leda till en uttalad symtombörda och försämrad hälsorelaterad livskvalitet (HRQOL). För många patienter leder hjärtrytmrubbning till osäkerhetskänsla och begränsningar i det dagliga livet. Förmågan att arbeta och möjligheten att planera för fritidsaktiviteter kan påverkas negativt. Det finns patienter som låter livet begränsas av sin hjärtrytmrubbning och de där fokus i tillvaron blir att hitta strategier för att förebygga och att kunna hantera sina besvär. Behandlingsalternativen kan vara flera. Valet står ofta mellan behandling med läkemedel eller radiofrekvensablation (RF-ablation) där behandling med RF-ablation kan vara botande för många patienter. Vid vård av patienter med hjärtrytmrubbning är det viktigt att kombinera objektiv utvärdering av patientens tillstånd med patienternas egna subjektiva upplevelser, detta för att kunna utvärdera i vilken omfattning hjärtrytmrubbningen påverkar livssituationen och om ytterligare behandling krävs för att minska symtombördan och förbättra HRQOL.

Det övergripande syftet med denna avhandling har varit att utvärdera symtombörda och HRQOL hos patienter med hjärtrytmrubbning samt att utveckla och utvärdera (validera) ett sjukdomsspecifikt frågeformlär anpassat för patienter med olika former av hjärtrytmrubbning.

Syftet i studie I var att beskriva patienternas HRQOL före behandling med RF-ablation och i studie II utvärderades patienternas HRQOL tre och tolv månader efter behandlingen. Studie I och II inkluderade patienter med två olika former av hjärtrytmrubbning remitterade för behandling med RF-ablation. Utvärderingen av patienternas HRQOL gjordes med två validerade, generella frågeformulär, SF-36 och EQ-5D, samt att patienterna besvarade några sjukdomsspecifika frågor i studie I. Patienternas HRQOL jämfördes i båda studierna med köns- och åldermatchade referensgrupper.
Syfte med studie III och IV var att utveckla och utvärdera (validera) ett sjukdomsspecifikt frågeformulär: **ASTA** (***A**rytmi**S**pecifikt frågeformulär vid **T**akykardi**A**ttack och hjärtrytmrubbning*) som utvärderar symtombörda och HRQOL hos patienter med olika former av hjärtrytmrubbning. Studie III och IV inkluderade patienter som skulle behandlas med elkonvertering, patienter med

förmaksflimmer som sökt akutsjukvård och patienter med olika former av hjärtrytmrubbning, remitterade för behandling med RF-ablation.

Studie I visade att patienterna skattade sin HRQOL signifikant lägre i sju av åtta skalor i SF-36 före behandlingen med RF-ablation i jämförelse med de köns- och åldermatchade referensgrupperna. Att ofta ha hjärtklappningsattacker (hjärtrytmrubbning) hade en uttalat negativ påverkan på HRQOL samt att vara kvinna och att vara äldre (≥50 år) var också faktorer som bidrog till försämrad HRQOL. Studie II visade att ett år efter behandling med RF-ablation var patienternas HRQOL återställd och på likvärdig nivå som den köns- och åldersmatchad referensgruppen, utvärderat med SF-36 och EQ-5D's index.

Det nya validerade ASTA-formuläret visade på tillfredställande psykometriska egenskaper i studie III och IV. Begreppsvaliditeten för både symtomskalan och skalorna som skattar HRQOL bekräftades med item-total korrelationer, konvergerande och diskriminerande validitet, samt med konfirmerande faktoranalys. Den interna konsistensen, utvärderad med Cronbach's alpha (α), var tillfredsställande inom alla skalorna, dvs. för ASTA's symtomskala och ASTA's total- och subskalor för HRQOL, med α varierande mellan 0.79 till 0.91.

Sammanfattningsvis visade resultaten från avhandlingen hur negativt påverkad patienternas tillvaro kan vara genom en uttalad symtombörda och försämrad HRQOL till följd av hjärtrytmrubbning. Behandling med RF-ablation återställde patienternas HRQOL till likvärdig nivå som den matchade referensgruppen. Det nya frågeformuläret ASTA visade på tillfredsställande egenskaper att kunna mäta symtombörda och HRQOL hos patienter med olika former av hjärtrytmrubbning.
För att på ett tillförlitligt sätt kunna utvärdera patienters subjektiva upplevelser av sin livssituation behövs frågeformulär som är utvecklade för och utvärderade i de patientgrupper där formuläret är avsett att användas.

ASTA-formuläret är det första validerade sjukdomsspecifika frågeformuläret för skattning av symtombörda och HRQOL, anpassat för patienter med de flesta former av hjärtrytmrubbning. ASTA kan därmed bli ett viktigt tillskott för utvärdering av livssituationen och behandlingseffekter för dessa patienter.

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APPENDIX 1

The ASTA questionnaire

The ASTA questionnaire is divided into three separate parts that can be used separately but preferably in a combination of all three parts.

ASTA background data

This part describes patient's demographics concerning; age, gender, cohabitant, level of education and pharmaceutical treatment.

ASTA symptom burden

This part evaluates commonly experienced symptoms in a symptom burden scale with nine different symptoms where a sum score is calculated for the items, where a lower score represents less symptom severity. Outside the symptom burden scale the patients are asked about: frequency of arrhythmia occasions and the duration, number of arrhythmia occasions during the last three months, to describe how the arrhythmia is experienced (palpitations), what factors that might influence arrhythmia appearance and about the experiences of near syncope and syncope in connection with the arrhythmia.

ASTA Health-Related Quality of Life

This part evaluates the arrhythmia's influence on daily life situations in a 13 item HRQOL scale, seven items in a physical subscale and six items in a mental subscale.

Recommendations for scoring of the ASTA questionnaire

General scoring information

ASTA symptom burden scale

ASTA symptom burden scale has nine items and a four point response scale with response alternatives from 0 to 3: “No (0), Yes, to a certain extent (1), Yes, quite a lot (2) or Yes, a lot (3) “. A sum score is calculated for the items, a higher score implies higher symptom burden due to the heart rhythm disturbance. Scoring for the ASTA symptom burden scale ranges from 0 (least burdensome) to highest 27 (most burdensome).

ASTA symptoms near syncope and syncope

The response alternatives are “No or Yes” for both the symptoms near syncope and syncope. The score is 0 for the answer “No” and with suggested score 3 to answer “Yes” to near syncope and score 6 for “Yes” to the most disabling symptom syncope (maximum score 6).

ASTA Health-Related Quality of Life

ASTA HRQOL scale has 13 items in the total scale describing the arrhythmia’s influence on daily life situation with a seven items physical subscale and six items mental subscale. The response score has the response alternatives ranging from: “No (0), Yes, to a certain extent (1), Yes, quite a lot (2), Yes, a lot (3)”. Scoring for the ASTA HRQOL total scale ranges from 0 (best possible HRQOL) to highest 39 (worst possible HRQOL). Higher scores reflect a more negative effect on HRQOL due to the heart rhythm disturbance. ASTA’s physical subscale ranges from 0 to 21 and the mental subscale ranges from 0 to18.

Transforming of scale scores

$$\text{Transformed scale} = \left[\frac{\text{actual raw score} - \text{lowest possible raw score}}{\text{Possible raw score range}}\right] \times 100$$

Scale	Number of items	Lowest and highest possible raw scores	Possible raw score range
ASTA symptoms; Symptom burden scale	9	0-27	28
ASTA symptom*; Near syncope	1	0-3	4
ASTA symptom*; Syncope	1	0-6	7
ASTA HRQOL; Total scale	13	0-39	40
ASTA HRQOL; Physical scale subscale	7	0-21	22
ASTA HRQOL; Mental scale subscale	6	0-18	19

Example:
ASTA symptom burden scale with a raw score of 13 would be transformed as follows:
$\left[\frac{13-0}{27}\right] \times 100 = 48$

Baseline assessment

Before any intervention all patients should be encouraged to fill out the total ASTA questionnaire, all three parts, to receive a baseline description of the patient's situation due to arrhythmia. Patients should be informed about reading the instructions on how to fill out the questionnaire thoroughly and to ask for help if so needed. Author's recommendation is to carefully check the ASTA questionnaire when it is handed in to ensure there are no missing data by mistake.

At follow-up

Patients should be recommended to carefully read the instructions at the end of part I, and to determine if they still have experiences of arrhythmia-related

symptoms and if any arrhythmia concerns influence their daily life (HRQOL). If they do not fill out parts II and III then they have a decided absence from arrhythmia–related impact. When patients consider no influence from arrhythmia and answer “No, I have no arrhythmia” at the end of part I then we recommend the scoring to be 0 (No symptom burden and No impaired HRQOL) for parts II and III if parts II and III are left without answers (blank).

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Patient ID	Datum för ifyllande	Tillfälle för ifyllande
		☐ Före beh. ☐1:a uppf. ☐2:a uppf.

Informationen ovan fylls i av vårdpersonal

(*A*rytmi*S*pecifikt frågeformulär vid *T*akykardi*A*ttack och hjärtrytmrubbning)

Arytmispecifika symtom
&
Hälsorelaterad livskvalitet vid hjärtrytmrubbning

Att leva med hjärtrytmrubbning (arytmi) kan innebära varierande grad av påverkan hos olika personer. Du som tillfrågas om att fylla i detta formulär ska eller har behandlats för någon form av hjärtrytmrubbning.

Antingen visar sig din hjärtrytmrubbning som attacker eller ihållande besvär, ex. hjärtrusningsattacker, förmaksflimmer, förmaksfladder eller rikligt förekommande extraslag.

Oberoende av vilken typ du har, kommer problemen med hjärtrytmen fortsättningsvis i detta frågeformulär benämnas som:

Hjärtrytmrubbning

Med formuläret **ASTA** vill vi kartlägga de symtom som din hjärtrytmrubbning kan medföra samt hur ditt liv och din hälsa påverkas.

Till dig som fyller i frågeformuläret ASTA

Utöver frågor om din hjärtrytmrubbning önskar vi svar på några andra frågor

Är du

- ❑ Kvinna
- ❑ Man

Din ålder är _____år

Vem eller vilka personer bor du tillsammans med?
(här kan du välja flera svarsalternativ)

- ❑ Ensamboende
- ❑ Maka/Make/ Sambo
- ❑ Barn

Annan:_____

Vilken är den högsta utbildningsgrad som du har avslutat?

- ❑ Mindre än grundskoleexamen (ex. folkskola)
- ❑ Grundskoleexamen eller motsvarande
- ❑ Gymnasieexamen eller motsvarande
- ❑ Högskoleexamen/Universitetsexamen

Vilken är din huvudsakliga sysselsättning?

_____

_____

_____

_____

ASTA del I

Hjärtrytmrubbning kan innebära varierande grad av påverkan hos olika personer. Vi vill att du med hjälp av följande frågor försöker beskriva hur du upplever det. Ange det svarsalternativ som passar bäst.

Fråga 1

När hade du senast hjärtrytmrubbning ?
*(Välj **ett** svarsalternativ)*

- ☐ Har ihållande hjärtrytmrubbning
- ☐ Har hjärtrytmrubbning av och till varje dag
- ☐ Mindre än en vecka sedan
- ☐ Mindre än 1 månad sedan
- ☐ 1 månad - mindre än 3 månader sedan
- ☐ 3 månader - mindre än 6 månader sedan
- ☐ 6 månader - mindre än 12 månader sedan
- ☐ Mer än 12 månader sedan

Fråga 2

a) Tar du några läkemedel ?

- ☐ Nej
- ☐ Ja

Om svar ”**Ja**” ber vi att du anger vilket/vilka läkemedel du tar regelbundet

b) Om du tar läkemedel **vid behov** för behandling av hjärtrytmrubbning ange vilket/vilka

- ☐ **Jag har hjärtrytmbesvär och fyller också i del II och III av formuläret**
- ☐ **Jag har hjärtrytmbesvär som jag inte känner av, men fyller i del II och III av formuläret**
- ☐ **Nej, jag har inte några hjärtrytmbesvär och fyller därför inte i del II och III av formuläret**

ASTA del II - Arytmispecifika symtom

Hjärtrytmrubbning kan variera beträffande hur ofta besvären kommer, hur länge de varar och vilka symtom man upplever. Vi vill att du med hjälp av följande frågor försöker beskriva din situation.
Ange det eller de svarsalternativ som passar bäst in på din situation.

Fråga 1

Hur lång tid <u>brukar</u> din hjärtrytmrubbning hålla på ?
*(här ska du välja **ett** svarsalternativ)*

- ☐ Mindre än 1 timma
- ☐ 1 timma - mindre än 7 timmar
- ☐ 7 timmar - mindre än 24 timmar
- ☐ 24 timmar - mindre än 2 dygn
- ☐ 2 dygn - 7 dygn
- ☐ Mer än 7 dygn

Fråga 2

Hur lång tid har din hjärtrytmrubbning varat <u>som längst</u> ?
*(här ska du välja **ett** svarsalternativ)*

- ☐ Mindre än 1 timma
- ☐ 1 timma - mindre än 7 timmar
- ☐ 7 timmar - mindre än 24 timmar
- ☐ 24 timmar - mindre än 2 dygn
- ☐ 2 dygn - 7 dygn
- ☐ Mer än 7 dygn

Fråga 3

Hur många tillfällen av hjärtrytmrubbning har du haft under de tre senaste månaderna ?
*(här ska du välja **ett** svarsalternativ)*

- ☐ Inga besvär alls
- ☐ Mindre än 5 tillfällen
- ☐ Mellan 5 och 15 tillfällen
- ☐ Mellan 16 och 30 tillfällen
- ☐ Mer än 30 tillfällen (men inte varje dag)
- ☐ Har hjärtrytmrubbning av och till varje dag
- ☐ Har ihållande hjärtrytmrubbning

Fråga 4

Känner du något av nedanstående i samband med hjärtrytmrubbning ?
*(här kan du välja **flera** svarsalternativ)*

- ☐ Hjärtat slår snabbt
- ☐ Hjärtat slår regelbundet
- ☐ Hjärtat slår oregelbundet
- ☐ Hjärtat slår hårdare än vanligt
- ☐ En känsla av att hjärtat hoppar över något eller några slag
- ☐ Korta episoder av hjärtrytmrubbning som varar mindre än 1 minut
- ☐ Nej, känner inte något av ovanstående

Fråga 5
Kommer din hjärtrytmrubbning vid speciella tillfällen?

☐ Nej
☐ Ja

Om svar ”**Ja**” ange gärna vid vilka tillfällen

Fråga 6

Vilka symtom upplever du i samband med hjärtrytmrubbning ?

a) Andfåddhet vid aktivitet

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

b) Andfåddhet även i vila

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

c) Yrsel

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

d) Kallsvettighet
(blek, kall, svettig)

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

e) Matthet/orkeslöshet

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

f) Trötthet

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

g) Bröstsmärta

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

h) Tryck/obehagskänsla i bröstet

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

i) Oro/ångest

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 7

Har du varit nära att svimma i samband med att du haft hjärtrytmrubbning ?

☐ Nej
☐ Ja

Fråga 8

Har du svimmat i samband med att du haft hjärtrytmrubbning ?

☐ Nej
☐ Ja

ASTA del III - Hälsorelaterad livskvalitet

Denna del av frågeformuläret handlar om hur din hjärtrytmrubbning påverkar ditt dagliga liv. Ange det svarsalternativ som passar bäst.
*(Om du känner dig tveksam ange det som stämmer för det mesta och om du upplever att du inte kan säga att hjärtrytmrubbningen påverkar det som frågas efter rekommenderar vi att du svarar **nej**)*

Fråga 1

Leder din hjärtrytmrubbning till att du inte orkar arbeta, studera eller utföra dagliga aktiviteter som du önskar?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 2

Leder din hjärtrytmrubbning till att du umgås med anhöriga och vänner mindre än vad du önskar?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 3

Leder din hjärtrytmrubbning till att du umgås med bekanta (personer du inte känner så väl) mindre än vad du önskar?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 4

Leder din hjärtrytmrubbning till att du undviker att planera saker som du annars gärna skulle vilja göra t.ex. resor eller andra fritidsaktiviteter?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 5

Leder din hjärtrytmrubbning till att din fysiska prestationsförmåga försämras?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 6

Leder din hjärtrytmrubbning till att din koncentrationsförmåga försämras?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 7

Leder din hjärtrytmrubbning till att du blir nedstämd eller ledsen?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 8

Leder din hjärtrytmrubbning till att du blir irriterad eller arg?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 9

Leder din hjärtrytmrubbning till sömnproblem?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 10

Leder din hjärtrytmrubbning till att ditt samliv/sexualliv påverkas negativt?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 11

Leder din hjärtrytmrubbning till att du känner rädsla för att dö?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 12

Leder din hjärtrytmrubbning till att din livssituation försämras?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

Fråga 13

När du inte har hjärtrytmrubbning, tiden mellan dina besvär, känner du då oro för att besvären ska komma tillbaka?

- ☐ Ja, mycket
- ☐ Ja, ganska mycket
- ☐ Ja, till viss del
- ☐ Nej

TACK för att du har tagit dig tid att fylla i formuläret !

Patient ID	Date of completion	Time of completion
		☐ Before treatment. ☐Follow-up 1 ☐Follow-up 2

The information above will be filled in by a member of health care staff

(Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia*)*

Arrhythmia specific symptoms & Health-related quality of life in connection with heart rhythm disturbance

Living with heart rhythm disturbance (arrhythmia), affects people in various degrees. If you are going to be, or have already been treated for any type of arrhythmia, we ask you to fill in this questionnaire.

Your arrhythmia manifests itself as attacks or persistent discomfort, e.g. palpitations, atrial fibrillation, atrial flutter or frequent extra heartbeats.

Irrespective of the type of problem you are experiencing, all heart rhythm issues in this questionnaire will be termed:

Arrhythmia

The **ASTA** questionnaire is aimed at mapping out the symptoms of your arrhythmia and how they affect your life and health.

For the person filling in the ASTA questionnaire

Besides answering questions regarding your arrhythmia, we would like you to answer some additional questions

Are you

- ❑ Female
- ❑ Male

You are _____years of age

Who do you live with?
(you can choose more than one alternative)

- ❑ Live alone
- ❑ Wife/Husband/ Cohabitant
- ❑ Children

Other:_____

What is the highest level of education that you have completed?

- ❑ Lower than compulsory school certificate(e.g. elementary school)
- ❑ Compulsory school certificate or equivalent
- ❑ Upper secondary school certificate or equivalent
- ❑ Higher education qualification/University degree

What is your main occupation?

_____

_____

_____

ASTA part I

Living with arrhythmia affects people in various degrees. By answering the following questions we would like you to describe your experience. Choose the alternative that corresponds the best to your situation.

Question 1

When did you last experience arrhythmia ?
*(Choose **one** alternative)*

- ☐ I have persistent arrhythmia
- ☐ I have arrhythmia on and off every day
- ☐ Less than a week ago
- ☐ Less than 1 month ago
- ☐ 1month – less than 3 months ago
- ☐ 3 months – less than 6 months ago
- ☐ 6 months – less than 12 months ago
- ☐ More than 12 months ago

Question 2

a) Are you currently on medication ?

- ☐ No
- ☐ Yes

If your answer is **"Yes"**, please note what medicine(s) you take on a regular basis

b) If you are on medication to treat arrhythmia **<u>when required</u>**, please note which one(s)

- ☐ **I suffer from arrhythmia and will complete part II and III of the questionnaire**
- ☐ **I have arrhythmia which does not affect me but I will complete part II and III of the questionnaire**
- ☐ **No, I do not suffer from arrhythmia and will therefore not complete part II and III of the questionnaire**

ASTA part II - Arrhythmia specific symptoms

Arrhythmia can vary in frequency, length of time and symptoms. By answering the following questions we would like you to describe your experience. Choose the alternative that corresponds the best to your situation.

Question 1

How long does your arrhythmia <u>normally</u> last?
*(please choose **one** alternative)*

- ☐ Less than1 hour
- ☐ 1 hour – less than 7hours
- ☐ 7 hours – less than 24 hours
- ☐ 24 hours – less than 2 days
- ☐ 2 days - 7 days
- ☐ More than 7 days

Question 2

What is <u>the longest time</u> you have experienced arrhythmia?
*(please choose **one** alternative)*

- ☐ Less than 1 hour
- ☐ 1 hour – less than 7 hours
- ☐ 7 hours – less than 24 hours
- ☐ 24 hours – less than 2 days
- ☐ 2 days - 7 days
- ☐ More than 7 days

Question 3

How many times have you experienced arrhythmia in the last three months?
*(please choose **one** alternative)*

- ☐ None
- ☐ Less than 5 times
- ☐ Between 5 and 15 times
- ☐ Between 16 and 30 times
- ☐ More than 30 times (but not every day)
- ☐ I experience arrhythmia on and off every day
- ☐ I suffer from persistent arrhythmia

Question 4

Do you experience any of the following in connection with your arrhythmia?
(you can choose more than one alternative)

- ☐ Heart beating fast
- ☐ Regular heartbeats
- ☐ Irregular heartbeats
- ☐ Heart beating harder than normal
- ☐ A sensation that the heart skips one or a few beats
- ☐ Short durations of arrhythmia that last less than 1 minute
- ☐ No, I do not experience any of the above

Question 5

Does your arrhythmia occur at specific times?

- ☐ No
- ☐ Yes

If your answer is ”**Yes**” , please note what time(s)

Question 6
What symptoms do you experience in connection with your arrhythmia?

a) Breathlessness during activity

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

b) Breathlessness even at rest

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

c) Dizziness

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

d) Cold sweat
(pale, cold, sweaty)

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

e) Weakness/fatigue

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

f) Tiredness

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

g) Chest pain

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

h) Pressure/discomfort in chest

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

i) Worry/anxiety

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 7

Have you ever felt faint in connection with your arrhythmia?

- ☐ No
- ☐ Yes

Question 8

Have you ever fainted in connection with your arrhythmia ?

- ☐ No
- ☐ Yes

ASTA part III – Health-related quality of life

This part of the questionnaire deals with how your arrhythmia affects your daily life. Choose the alternative that corresponds the best to your situation.

*(If in doubt, please choose the alternative that mostly corresponds to you. If you feel that you cannot determine whether your arrhythmia affects the requested aspect of your life, we recommend that you answer **no**).*

Question 1

Do you feel unable to work, study or carry out daily activities as you would like to due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 2

Do you spend less time with your relatives and friends than you would like to due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 3

Do you spend less time with acquaintances (people you do not know that well) than you would like to due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 4

Do you avoid planning things you would like to do, for instance travelling or leisure activities due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 5

Is your physical ability reduced due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 6

Is your ability to concentrate reduced due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 7

Do you feel low-spirited or sad due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 8

Do you feel irritated or angry due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 9

Do you suffer from sleep problems due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 10

Is your sexual life affected negatively by your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 11

Are you afraid of dying due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 12

Has your life situation deteriorated due to your arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Question 13

Do you feel worried that your symptoms will re-occur during the periods when you do not suffer from arrhythmia?

- ☐ Yes, a lot
- ☐ Yes, quite a lot
- ☐ Yes, to a certain extent
- ☐ No

Thank you for your time !