Are sleep-related breathing disorders part of the syndrome of chronic heart failure?

An observational study

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DEMARCATION

This thesis is an exam document in the Master of Primary Care Medicine program and is the work of two authors. We explicitly chose not to divide the work in two separate parts, as this would substantially compromise the structure of the paper and, more importantly, the essential integration of both trails in the conclusion. Nonetheless, we understand that for the purposes of evaluation we need to stipulate the main focus of each author separately and would like to commence by doing so.

ALEXANDER SMETS focussed on the interaction between heart failure symptoms and comorbidities on one hand and somnolence caused by a decrease in sleep quality on the other, thus influencing screening questionnaires' predictive values. In the literature study, he elaborated the properties of the questionnaires, their predictive values, and the proposed physiological interaction between OSAHS and chronic heart failure.

STEVEN DEKEYE aimed at estimating the prevalence of sleep-related breathing disorders in the chronic heart failure population by means of an ambulatory sleep monitor and the correlation of the measured sleep parameters and subjective sleep quality measured with questionnaires. As for the background and literature study, he mainly focussed on the reported prevalence of OSAHS and the technical properties and predictive values of Somnolter®, compared to the gold standard.

The home visits with questionnaire and sleep monitor assistance were made by both authors, according to whether they were attending physicians of the patient. The integration and comparison of the sleep monitor registrations and the results of the questionnaires was, for obvious reasons, performed in equal collaboration, according to the emphasis as described above.

“Now cracks a noble heart. Good night, sweet prince,

And flights of angels sing thee to thy rest!”

Hamlet, V.2.351-352

We would like to thank our promotor, prof. dr. Degryse for his guidance and cooperation in this project.

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Are sleep-related breathing disorders part of the syndrome of chronic heart failure? – An observational study

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ABSTRACT

Background: Previous research has shown that there is a higher than normal prevalence of sleep-related breathing disorders in diseases that cause fluid retention. In heart failure patients, hypoxia, intrathoracic pressure disturbances and sympathetic nervous system overdrive can deteriorate myocardial contractility, while rostral fluid shift due to water retention induces these defects. This study, which builds on a previous pilot project, investigates the sleep apnoea prevalence in the chronic heart failure population and the question whether a systematic screening in this population might be beneficious.

Methods: We screened 43 chronic heart failure patients for obstructive sleep apnoea disorder with an ambulatory sleep monitor. We also asked them to complete seven questionnaires on somnolence, fatigue, sleep quality and overall perceived health status. Some of these are specifically designed for OSAHS screening and we compared the scores on these with the sleep monitor results, to assess their predictive values.

Results: 76.74% of all patients that we screened with Somnolter® (n = 43) had more than 5 obstructive events per hour. In total, 44.19% of the participants had mild, 23.26% moderate, and 9.30% severe OSAHS. The sleep quality questionnaires' predictive values are low in this specific population and the scores poorly correlate with the measured sleep disturbance.

Conclusion: Based on our results, it seems that sleep-related breathing disorders are indeed part of the chronic heart failure syndrome. Our most conservative estimation of the prevalence of OSAHS in this population is 32.56%, which is substantially higher than the estimated overall prevalence. Furthermore, we demonstrated the poor predictive values of questionnaires in screening for OSAHS in the chronic heart failure population and cannot recommend them for this purpose. Physicians should consider the possible benefits of early OSAHS detection to prevent preliminary deterioration of the cardiac function and loss of quality of life.

BACKGROUND

Situation

Recent studies have found a link between chronic heart failure and sleep-related breathing disorders, specifically obstructive sleep apnoea and hypopnoea disorder (OSAHS). This is a relatively new field of research and, to explore this correlation further, we recently conducted a small-scale pilot study into this subject.[1] This study builds on the design we elaborated two years ago, with a fine-tuned methodology and larger study population.

While most primary care physicians are familiar with chronic heart failure, sleep-related breathing disorders are not frequently treated in a non-pulmonology setting and we will therefore begin this introduction by giving a concise overview of the major key points of sleep

apnoea. After that, we shall describe the pathophysiological mechanisms that may lie at the basis of the interaction between chronic heart failure and OSAHS.

Sleep apnoea syndrome

Sleep apnoea syndrome can be divided in three major phenotypes: central sleep apnoea and hypopnoea syndrome (CSAHS), obstructive sleep apnoea and hypopnoea syndrome (OSAHS) and mixed sleep apnoea and hypopnoea syndrome (MSAHS). A central sleep apnoea event is a cessation of airflow because of a lack in respiratory effort, caused by a malfunction of the feedback mechanisms in the pre-Bötzinger complex of the ventral respiratory centre in the medulla oblongata. Obstructive sleep apnoea, on the other hand, is a suppression of the airflow caused by a mechanical obstruction with a preserved respiratory effort. Mixed sleep apnoea disorder is the simultaneous occurrence of both mechanisms.

Definitions

The definition of **apnoea** is a cessation of airflow for over 10 seconds, whereas an **hypopnoea** is a reduction of 30% or more of the airflow combined with either a drop in 4% or more from the baseline oxygen saturation level, or a fragmentation of sleep because of an arousal. A **respiratory event related arousal** (RERA) is a period of minimal 10 seconds, in which there is an increased respiratory effort, resulting in a progressive drop in oesophageal pressure, followed by an abrupt return to normal with a micro-arousal, not meeting the criteria for an apnoea or hypopnoea. We remark here that the gold standard for the measurement of a RERA requires an oesophageal manometry. However, an indirect measurement of the intra-thoracic pressure through the pulse transit time with a pulse-oximeter has been validated as a reliable way of measuring RERAs and both for practical considerations and the patients' comfort, this is the most used method in sleep laboratories.[2, 3] For evident reasons, this is also the method used in an ambulatory sleep study. The **apopnoea-hypopnoea index** (AHI) indicates the mean occurrence of apnoeas and hypopnoeas during a night and is used to classify the OSAHS as either mild (5-15 events per hour), moderate (15-30 events per hour) or severe (> 30 events per hour)[4]. Finally, the **respiratory disturbance index** is the mean number of apnoeas, hypopnoeas and RERAs per hour of sleep.

Epidemiology

The obstructive sleep apnoea disorder prevalence in the general population is estimated in the order of magnitude of 2 to 4%[5], but several studies suggest that OSAHS is largely

underdiagnosed, because of the unspecific cluster of symptoms, if any are noticed and mentioned by the patient. Young et al. (1997) have suggested that up to 93% of women and 82% of men with moderate to severe OSAHS are not clinically diagnosed.[6]

Prevalence rates are greatly influenced by several risk factors for OSAHS and this results in significant differences between various patient groups.[7, 8] In general, men are twice as often affected as women and higher age, obesity, family history, menopause, craniofacial anomalies, medical comorbidities, smoking and alcohol also result in a higher risk for obstructive sleep apnoea disorder. Many of these risk factors are also abundant in the chronic heart failure population, which is of interest for our dissertation. Of all risk factors for OSAHS, obesity is the strongest. More than 60% of patients presenting in a sleep laboratory have excess body weight[9] and Young et al. found that 58% of the moderate to severe sleep apnoea and hypopnoea disorders are attributable to a BMI higher than 25 kg/m².[10] More recently, OSAHS has also been associated with multiple cardiovascular diseases, among which systemic hypertension, cardiac arrhythmia and ischemic heart diseases. It has been assessed that the prevalence of OSAHS rises to 50% in certain of these comorbidities, more specifically those associated with sodium and water retention.[11]

Physiology

As to this point it is not known if there is a direct and causal relationship between OSAHS and chronic heart failure, and through which mechanisms it might work. Although several mechanisms of action have been proposed to explain the correlation, none has conclusively been proven to be responsible for it, due to the heterogeneous study populations and the various comorbidities (e.g. hypertension, obesity,...) related with chronic heart failure.[12] Nonetheless, strong arguments for a bidirectional relationship between chronic heart failure and sleep-related breathing disorders have come forth from recent research. Establishing the causal relationship and its direction reaches beyond the goal of this study and is a focus for further research. We will nonetheless briefly discuss the proposed physiological mechanisms, for which we have to take a look at the three pathophysiological mechanisms that cause sleep-related breathing disorders; upper airway instability, respiratory control instability and respiratory pump disorders.[13] All three influence, and are influenced by, the state of the cardiovascular system, as we shall see below.

Upper airway instability

Unlike the trachea and bronchi, the pharynx consists of muscle and soft tissue without any structural support of cartilaginous tissue and is therefore prone to collapse. Obese individuals

have a substantial amount of pharyngeal fat deposition, which facilitates upper airway narrowing and collapse. Other causes of a narrow upper airway are retrognathia, tonsillar hypertrophy and macroglossia. Specifically in heart failure patients, fluid accumulation mechanically influences the upper airway. In supine position, a fluid shift from the legs towards the neck causes the neck veins to expand thereby inducing formation of oedema in the surrounding soft tissue. This gives a significant pressure on – and thereby possible obstruction of – the upper airway tract.[14]

Respiratory pump disorders

The lung volume depends of the posture and sleep/wake state. When in upright position, we see a greater ventilation at the apices and a better perfusion at the bases. A supine position results in a lower end-expiratory lung volume and a greater VQ mismatching.[15] A state of sleep gives a supplementary reduction (infra). Comorbidities like obesity or cardiac pathologies will enforce this physiologic effect and result in an even greater reduction.

Respiratory control instability

While awake, the respiratory system is controlled by three main factors; cortical (so the breathing is synchronized with speech, eating, vocal expressions,…), neural and metabolic. While asleep, the first two (cortical and neural) are switched off, so only the metabolic drive remains. This works with a negative feedback system in which information from the lungs will be received by the brain after about 10 seconds, which is the normal time blood needs to leave the pulmonary veins and reach the peripheral chemoreceptors. This can take up to 30 seconds in patients with an impaired cardiac output.[16]

Contrariwise, OSAHS might contribute to heart failure by exposing the cardiovascular system to intermittent hypoxemia. This hypoxemia results in a reduction in oxygen supply to the myocardium, which, when long-existing, compromises contractility. Low blood oxygen levels also instigate an increase in sympathetic nervous system activity, which causes elevation of the cardiac preload through sodium and water retention via the renin-angiotensin pathway. Next to that, the unbalanced surges in negative intra-thoracic pressure, increase the cardiac afterload. All these mechanisms negatively influence the progression of heart failure and form a vicious circle that worsens both the cardiac an respiratory pathology.[17, 18]

Significance

With an increasing life expectancy, we may expect a rising incidence of cardiac disease and all of its complications and an early detection of these is warranted to reduce morbidity and mortality. Specifically for sleep apnoea, Marin et al. (2005) demonstrated that OSAHS increased the risk of both fatal and non-fatal cardiovascular events and that CPAP treatment reduced this risk. Where the incidence of non-fatal cardiovascular events in the severe untreated patient group was 2.13 per 100 person years for non-fatal events, CPAP treatment reduced this number to 0.35 per 100 person-years, which was just slightly above the 0.30 incidence rate in the healthy participants group.[19] Another observational study, by Anandam et al. (2013), demonstrated that treatment of OSAHS with either a mandibular adjustment device (MAD) or CPAP reduced the incidence of fatal cardiovascular events from 2.1 per 100 person-years to 0.61 and 0.56 per 100 person-years, respectively.[20] It is therefore important that we identify as many risk factors as possible that negatively influence the progress of heart failure, in order to prevent the often severe comorbidity and loss of quality of life that is seen with this disease. Still, the impact of CPAP treatment on the disease progress and quality of life in chronic heart failure, specifically, is yet to be established and might be the subject of a future prospective study.

Study goal

The aim of this study is to establish the prevalence of sleep-related breathing disorders in the chronic heart failure population. It builds further on a pilot study we conducted recently, in which we discussed the feasibility and most relevant methods to screen for sleep-related breathing disorders the chronic heart failure population in the primary care setting. In this previous study, we used a number of questionnaires and two home monitoring devices: Brizzy® and Somnolter®. Nine out of ten patients with clinical and echocardiographically confirmed heart failure tested positive for OSAHS with a home monitor device. We also found clues that the sensitivity and specificity of the most currently used questionnaires are probably insufficient to be used as screening methods for the detection of sleep apnoea in chronic heart failure patients, because they cannot reliably distinguish somnolence (a sleep apnoea symptom), and fatigue (a chronic heart failure symptom). It has been suggested that the difference between somnolence and fatigue is not very clearly distinguishable for most people and that patients who are used to being weary rapidly because of their heart failure, do not easily indicate somnolence problems. Furthermore, questionnaires are prone to a significant interpretative variability, compromising their reliability. We compare the results of the questionnaires with the

Somnolter® measurements to assess their predictive values, thereby evaluating if they are suitable screening instruments for OSAHS in the chronic heart failure population.

METHODS

Sampling

As in our pilot study, we screened the electronic medical files of primary care practices for patients with chronic heart failure by means of coded diagnosis in the medical software. We screened four extra primary care practices, thus begetting a pool of six practices. We then filtered out all patients who had undergone a cardiac ultrasound and compared their test results with the inclusion criteria, as defined below.

Inclusion and exclusion criteria

We included all patients with clinical symptoms of chronic heart failure in whom the diagnosis had been echocardiographically confirmed, based upon the guidelines of the European Society of Cardiology for chronic heart failure.[21] The clinical criteria are listed in the table below. A clinical diagnosis of heart failure requires the presence of either at least two major criteria, or at least one major criterium with two or more minor criteria.

CLINICAL DIAGNOSIS OF HEART FAILURE	
MAJOR CRITERIA	**MINOR CRITERIA**
Paroxysmal nocturnal dyspnea	Peripheral edema
Orthopnea	Nightly cough
Elevated central venous pressure	Dyspnea on exertion
Third heart sound / ventricular gallop	Hepatomegaly
Cardiomegaly (X-ray)	Pleural effusion
Pulmonary edema (X-ray)	Heart rhythm > 120bpm
	Weight loss > 4.5 kg in 5 days

The echocardiographic inclusion criteria are as follows: either systolic heart failure with LVEF < 50%, EDV LV > 97 mL/m2, ESV LV > 43mL/m2 or diastolic heart failure with LVEF > 50% without LV dilatation and with é < 8 cm/s septal, é < 10 cm/s lateral or mean é < 9cm/s, E/A ratio < 1 or E/é ratio > 15. Both sets are applicable in combined heart failure. The inclusion criteria are identical to those of our pilot study.

ECHOCARDIOGRAPHIC INCLUSION CRITERIA	
Systolic heart failure	**Diastolic heart failure**
Left ventricle ejection fraction < 50%	**Delayed diastolic relaxation** • Decreased e' (< 8 cm/s septal or < 10 cm/s lateral or < 9 cm/s average) • E/A < 1
End-diastolic left ventricle volume > 97 mL/m²	**High left ventricular filling pressure** • E/e' > 15 • E/A > 2 • [A_{pulm}-A_{mitr}] duration > 30 ms
End-systolic left ventricle volume > 43 mL/m²	

Patients with an ongoing episode of acute heart failure and / or cognitive impairment (Mini Mental State Examination score < 20) were excluded, since they would not have been able to complete the questionnaires

We also included the patients from our pilot study who were tested with Somnolter®, since they were sampled in the same way and met the same inclusion criteria.

Patient recruitment

We contacted all patients who met the criteria, either by phone or in person during a visit to the practice. We explained the aim and practical course of the study and gave them an informative brochure and informed consent (which can be found in appendix 3). Afterwards, we planned a visit at home for sleep monitoring with the Somnolter® device and the completion of the questionnaires. Of the 75 patients who met the inclusion criteria, 16 were excluded because they met at least one of the exclusion criteria. Of the 59 remaining, 44 patients gave their consent to participate, while 15 patients refused. Unfortunately, one patient who had agreed to enrol, passed away before the home monitoring started. An algorithm with the precise numbers is concluded in the appendage.

Home visit

A few hours before the patients went to bed, we visited them at home to attach the sleep monitor and to do a clinical examination in which we assessed the following parameters: neck and abdominal circumferences, weight, length and BMI. Neck circumference was measured

mid-cervical, just below the prominentia laryngea. The abdominal circumference was measured half-way between the tenth rib and the spina iliaca anterior superior. The patients received the seven questionnaires to fill in during the home visit. The device was installed by a researcher and the patients were asked to activate it right before they went to bed. The following day, we retrieved the device and asked about the quality of sleep and the perceived impact of the device on the patient's sleep quality.

Questionnaires

We selected seven questionnaires based on frequency of use and validation in other studies to make a representative assessment of five relevant domains for the study population: quality of life, quality of sleep, daytime sleepiness, specific symptoms of OSAHS (snoring and breathing pauses during the sleep) and symptoms of chronic heart failure. We compared the results of the questionnaires with the results of the ambulatory sleep monitor to evaluate their performance as screening tools. Because of copyright restrictions, we have not included the questionnaires in the appendices. References to the used versions are included below.

Nottingham Health Profile

The Nottingham Health profile is a general quality of life questionnaire that measures the patient-perceived emotional, social, physical and psychic well-being. It is an instrument that has proven to be a useful tool for the assessment of a person's subjective, i.e. perceived, health status. It can be used to evaluate the evolution of illness and the effects of therapy. [22] [23] It consist of 38 yes-no questions covering six domains: energy level, pain, emotional status, social isolation, physical abilities and sleep. We used the validated Dutch version by Passchier and Erdmann (1993). All domains are evaluated separately and the results are summarised in an overall score. The maximum score on each of the domains is 100. The higher the score, the more severe problems are perceived by the patient.

Berlin Questionnaire

The Berlin Questionnaire was designed as a primary care setting tool to screen for the presence of sleep disturbance disorders. It consists of ten yes-no questions plus information on height and weight. It is divided into three categories. Positive scores in 2 or more categories suggest that the patient has a high risk for sleep apnoea. Netzer et al. (1999) found that the high risk category predicted a respiratory disturbance index greater than 5 with a sensitivity of 86% and a specificity of 77%.[24] Recent research by Senaratna et al. (2017) has confirmed that

outside the sleep clinic population it indeed has high sensitivity, with lower specificity, significantly varying between different populations. [25] The questionnaire was translated into Dutch and validated by Zwolsman et al. [26]

STOP-BANG

The STOP-BANG Questionnaire is a screening tool that consists of 8 yes-no questions for the screening for obstructive sleep apnoea. These comprise snoring, daytime sleepiness, observed breathing pauses, hypertension, BMI > 35, age > 50 years, neck circumference > 43 cm (men) or > 40 cm (women) and gender. A score of 0 – 2 is considered as low risk for OSAHS, while scores of 3 – 4 and 5 – 8 indicate an intermediate and high risk, respectively.[27] While sensitivity with the ≥ 3 threshold is high (up to 93%), specificity is low (37 to 47%), thereby resulting in relatively high numbers of false-positive results.[28] Nonetheless, a recent validation study confirmed its practical use; the higher the STOP-BANG score, the higher the risk for obstructive sleep apnoea.[29] The questionnaire has a validated Dutch version.[30]

Epworth Sleepiness Scale

The Epworth Sleepiness Scale is an instrument to measure daytime sleepiness. It is a short questionnaire that asks the patient to estimate the odds that he or she would fall asleep in eight everyday life situations. Each situation is scored from 0 to 3, with the higher the score, the higher the chance to doze off. A score higher than 9 indicates abnormal daytime sleepiness and an increased risk of sleep apnoea.[31] Scores higher than 15 indicate a high risk for severe sleep apnoea syndrome or narcolepsy. The ESS has a validated Dutch version and is since long widely used as a screening instrument for sleep disorders and as a follow-up tool in the treatment of OSAHS.[32]

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index is a standardized sleep questionnaire, consisting of 19 questions scaled from 0 to 3 to assess the subjective sleep quality. This questionnaire is not specifically designed for OSAHS, but rather assesses overall subjective sleep quality. It is the most variated sleep questionnaire and it has shown strong reliability and validity, which makes it a useful tool in the diagnosis and follow-up of sleep disturbances, both in somatic and psychiatric disease. The questions cover subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medication and daytime dysfunction. Besides, there are 5 additional items that are completed by a bed partner or

roommate. The global score ranges from 0 to 21, with higher scores predicting greater sleep disturbance. A total score of 5 or higher is an indication of poor sleep quality. To our knowledge, no validated Dutch version exists, so we used a translation from the original questionnaire in English.

Minnesota Living with Heart Failure Questionnaire

The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a more subjective and disease-specific questionnaire that measures the self-reported health-related quality of life. It's a list of 21 items about exercise and effort for daily activities, these items are scored from 0 to 5, where the higher the score, the poorer the quality of life. It is a valid instrument, that produces reliable scores, making it widely used to assess the impact of chronic heart failure on the quality of life. The Dutch version was validated by Wijbenga et al. in 1998.[33]

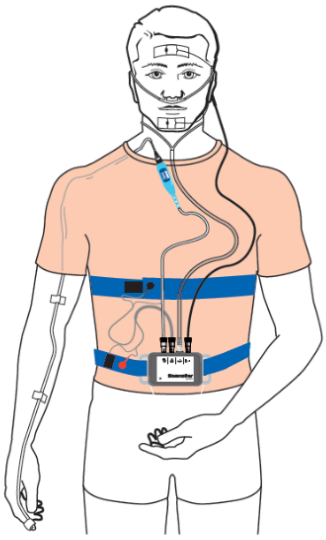
Left Ventricular Dysfunction Questionnaire

The Left Ventricular Dysfunction Questionnaire is a short questionnaire specific for patients with chronic heart failure based on left ventricular dysfunction and consists of 36 true or false questions about the impact of heart failure on everyday life. It is strongly related to the questions of the MLHFQ. The sum of the true responses is translated to a percentage, with 100 percent being the worst and 0 the best score. It's a reliable and valuable test that is very useful in the follow-up of chronic heart failure patients to evaluate the impact on the quality of life and the impact of treatment, because it clearly responds to changes in health status.[34] We found no Dutch form of this questionnaire and used a translated version from the original.

Sleep monitor

Somnolter® is an ambulatory sleep recorder that registers six parameters: nasal airflow, respiratory motion of the thorax and of the abdomen, mandibular movements, oxygen saturation and pulse rate. Its mechanism is based on Jawac® technology, which registers the midsagittal jaw movement by measuring the distance between a sensor on the forehead and a sensor on the mandible. This allows to identify a certain pattern that occurs during respiratory effort, which is characterized by a gradual opening mandibular movement, followed by a swift mouth closing gesture whilst the normal breathing pattern recovers. [35 36]

This technology has proven to be successful in identifying sleep apnoea disorder; Senny et al. found a sensitivity of 88.6% and a specificity of 83.6% for the automated analysis of the Jawac® sensor alone. [37]



Somnolter® with the Jawac® sensors on the chin and forehead, the nasal flow meter, the pulse oximeter and the belts that register the abdominal and thoracic distention.

When there is an episode of apnoea or hypopnoea, the report shows a desaturation and decrease of nasal air flow, followed by a discrepancy between abdominal and chest movement. Respiratory event related arousals are measured with the pulse-oximeter, using the pulse transit time as an extrapolation for the intrathoracic pressure. As we already discussed above, this is a validated method of establishing the intrathoracic pressure. Since Somnolter® cannot register an EEG, it can only estimate arousals based upon respiratory and pulse rate patterns. This implies that only the hypopnoeas resulting in a sufficient decrease in oxygen saturation from the baseline are actually measured, while those resulting in arousal or sleep fragmentation, can only be detected indirectly through pulse en respiratory rate variation. The analysis therefore differentiates the measured AHI (mAHI) from the estimated (eAHI). We analysed both data, but have only taken the measured value into account for the diagnosis of sleep apnoea syndrome, as was done in the studies into the predictive values of Somnolter®. Via the aforementioned changes in heart rate and breathing and the patient's position, Somnolter® can also automatically discriminate between awake and asleep by recognition of specific heart rate and respiratory patterns. This is important, because it gives a more precise value for the AHI, since data retrieved while the patient is awake, are not taken into account. Senny et al. demonstrated that an accurate registration of the total sleeping time gives a more precise value for the sleep disorder index, reducing the risk of underestimation.[38] All measured parameters can be analysed the next day by the Somnolter® software's algorithm, but are also separately registered and displayed, so they can be reviewed and checked afterwards. The fully automatic procedure takes about 10 minutes for an analysis protocol.

The choice for a home monitoring device is a practical one. First, most heart failure patients are of a certain age and have reduced mobility, which increases the threshold for extensive testing in a hospital setting.[39] Secondly, polysomnography is not widely available and long waiting lists with a delay up to several months are the rule rather than the exception. Somnolter® is not only more readily available, it also has a significantly lower running cost. Thirdly, polysomnography implies an inpatient setting and more sensors attached to the body,

which might compromise sleep quality. However, it is yet to be investigated if this is a disadvantage compared to the outpatient home monitoring setting and in how far this is significant. Further below, we included the scores for the perceived sleep quality during a night with Somnolter® in order to make a preliminary assessment.

Somnolter® has proven to be a useful tool, because it has high sensitivity and specificity next to polysomnography, which is the gold standard for sleep disorder diagnosis. A clinical study by Cheliout-Heraut et al. on ninety patients compared the use of Somnolter® to polysomnography for the diagnosis of obstructive sleep apnoea syndrome. They found a correlation of 0,95 with a sensitivity and specificity of respectively 83.6% and 81.8% in auto analysis mode, which we correspondingly used in this study.[40] These high predictive values in combination with the ease of use and relatively low operating costs, make it a promising method for home monitoring in a primary care setting.

Analysis

For the analysis of the results, we used Bayesian statistics and correlations were determined using Pearson's correlation coefficient formula. The interpretation was based on the Evans (1996) guidelines.[41]

ETHICAL

This study was evaluated and approved by the ethical committee of the KU Leuven University Hospital in March 2017. All patients agreed on participating in this study and signed an informed consent. The applicable documents can be found in the appendices (appendix 1 – 3).

RESULTS

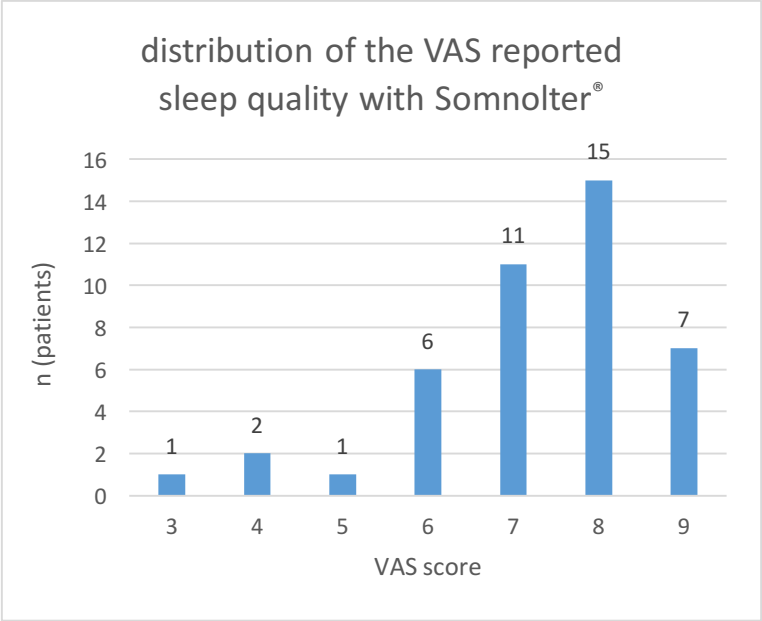
Somnolter®

We screened 43 heart failure patients for OSAHS, using questionnaires and an ambulatory sleep monitor. The male to female ratio was 3.77 and the mean age of our patients was 78.33 years. We found a prevalence of 76.74% for mild to severe OSAHS, using the measured AHI by Somnolter®. When making use of the estimated AHI, this number rose to 95.35%. The prevalence rate in the moderate to severe group was 32.56% for the mAHI, rising to 72.09% using the eAHI. The numbers resulted in a mean mAHI of 13.56 (± 3.06) and a mean eAHI of 24.05 (± 3.49). The mean respiratory disturbance index was 31.75 (± 4.15) and the mean of

the minimum oxygen saturation was 80.33% (± 2.73%), with values varying between 55% and 94%.

SOMNOLTER® RESULTS				
OSAHS severity	**mAHI**		**eAHI**	
	(n)	**%**	**(n)**	**%**
no OSAHS	10	23.26	2	4.65
mild	19	44.19	10	23.26
moderate	10	23.26	17	39.53
severe	4	9.30	14	32.56

The instalment of Somnolter® proved to be very user-friendly and was a matter of a few minutes. Two measurements had to be repeated; one because the pulse-oximeter came loose, the other because of a software dysfunction, which was solved by resetting the monitor. Somnolter® is generally well tolerated; 37.21% of patients found the monitor inconvenient, but the impact on the sleep quality seemed rather limited with 69.77% of patients reporting having slept well. The mean VAS score for sleep quality was 7.26 (± 0.42) on a maximum of 10, ranging from 3 to 9, with a tendency toward the higher scores, as depicted in the graph on the right. The most reported nuisances are the pressure of the pulse-oximeter on the finger and the light of the pulse-oximeter.



Questionnaires

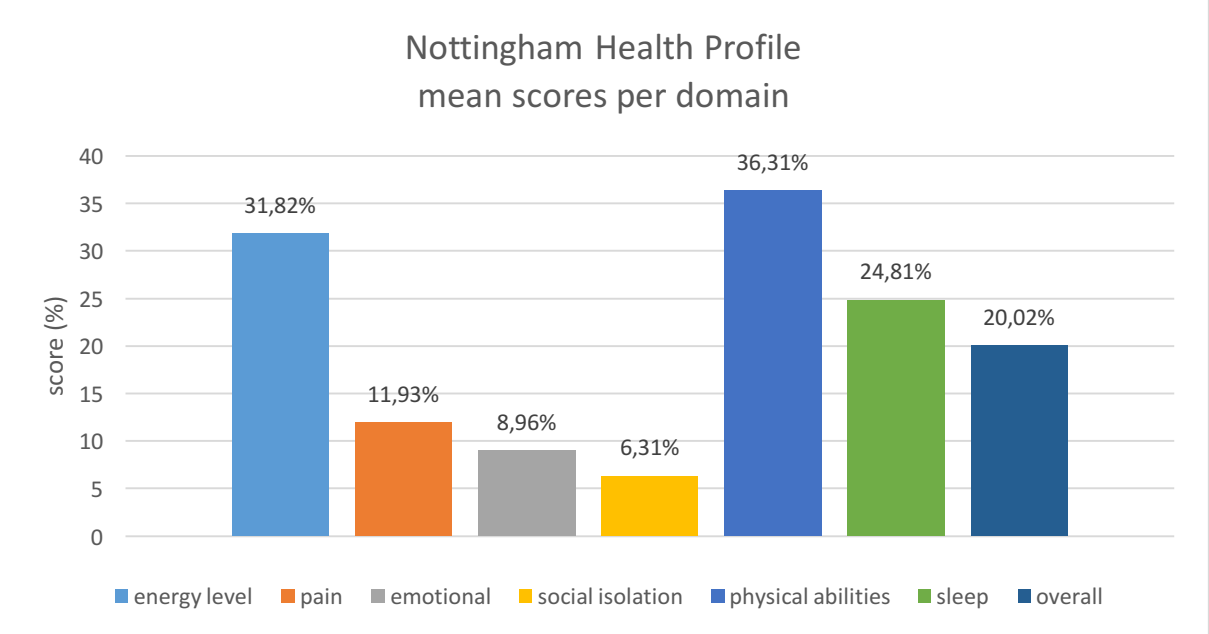
As for the questionnaires, we assisted the patients while they filled in the forms, in order to ascertain that they were entirely completed. This proved to be a strenuous and time-consuming task for both the patients and the researchers, not only because of the extend of our questionnaire set, but also because of the fact that a lot of patients were puzzled by certain

questions, notably those that did not obviously apply to themselves or their environment (see *Discussion*), or by questions that asked to estimate a clearly defined figure (notably the PSQI enquires about mean duration of sleep, bed time, sleep latency duration, etc.).

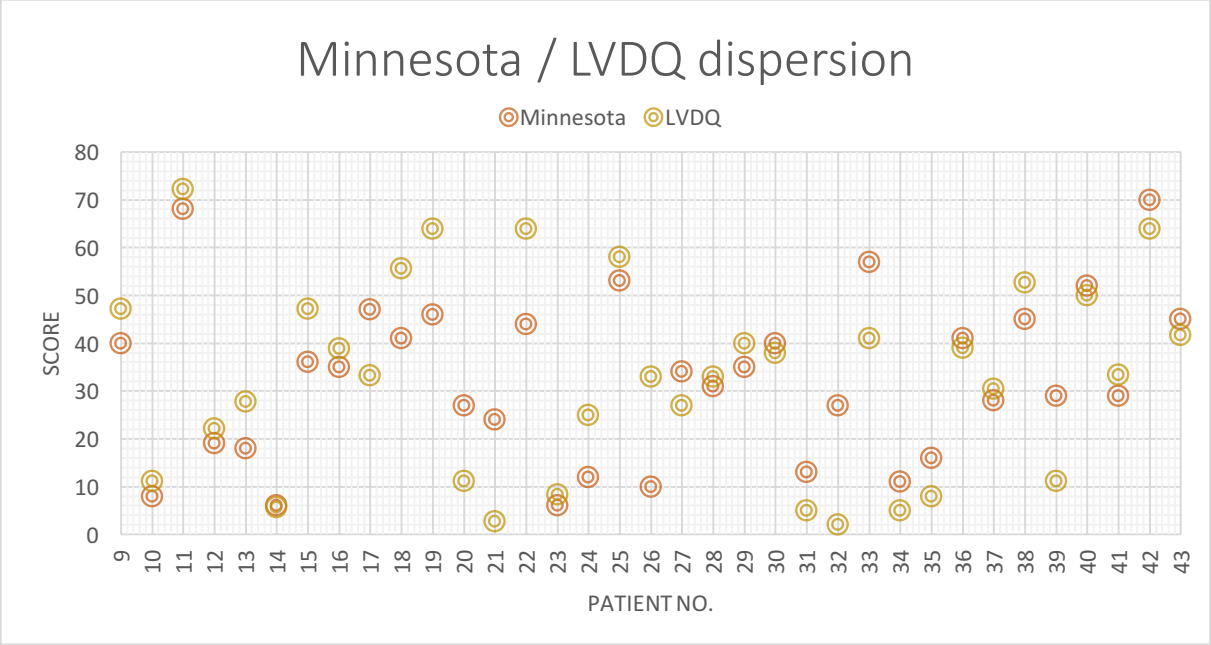
The results of the OSAHS- and sleep-specific questionnaires are summarised in the table below by means of their sensitivity, specificity, positive predictive value and negative predictive value next to the measured AHI with Somnolter®. We used the proposed cut-off values (v*ide supra*), except in the STOP-BANG questionnaire, where we made use of the ≥ 5 threshold (see *Discussion*).

QUESTIONNAIRE	***Sensitivity (%)***	***Specificity (%)***	***PPV (%)***	***NPV (%)***
Berlin	67.65	66.67	88.46	35.29
STOP-BANG	68.75	36.36	75.86	28.57
ESS	36.36	60.00	75.00	22.22
PSQI	60.61	60.00	83.33	31.58

The Nottingham Health Profile had a mean overall score of 20.02 (± 3.92). The mean scores of the different domains are depicted in the graph below. The higher scores, the more problems are perceived by the patient.



For the Minnesota Living With Heart Failure Questionnaire, we found a mean score of 32.66 (± 5.63) and for the Left Ventricular Dysfunction Questionnaire a mean score of 32.81% (± 6.73%). Mind that these two questionnaires were not included in our pilot study, so n = 35. A dispersion graph that compares both questionnaires is given below.



Follow-up

The results of the sleep study were discussed with the patient by their attending physician. The severity of the impact on everyday life was assessed by anamnesis and the study's questionnaires. Possible further investigations and treatment options were discussed with the patient, where apt. One patient with a positive result underwent a polysomnography afterwards, which revealed a AHI of 36.0. This was very close to the estimated AHI of 34.7 by Somnolter®. On the other hand, it is worth noting that the measured AHI of 19.4 was a significant underestimation of the OSAHS severity.

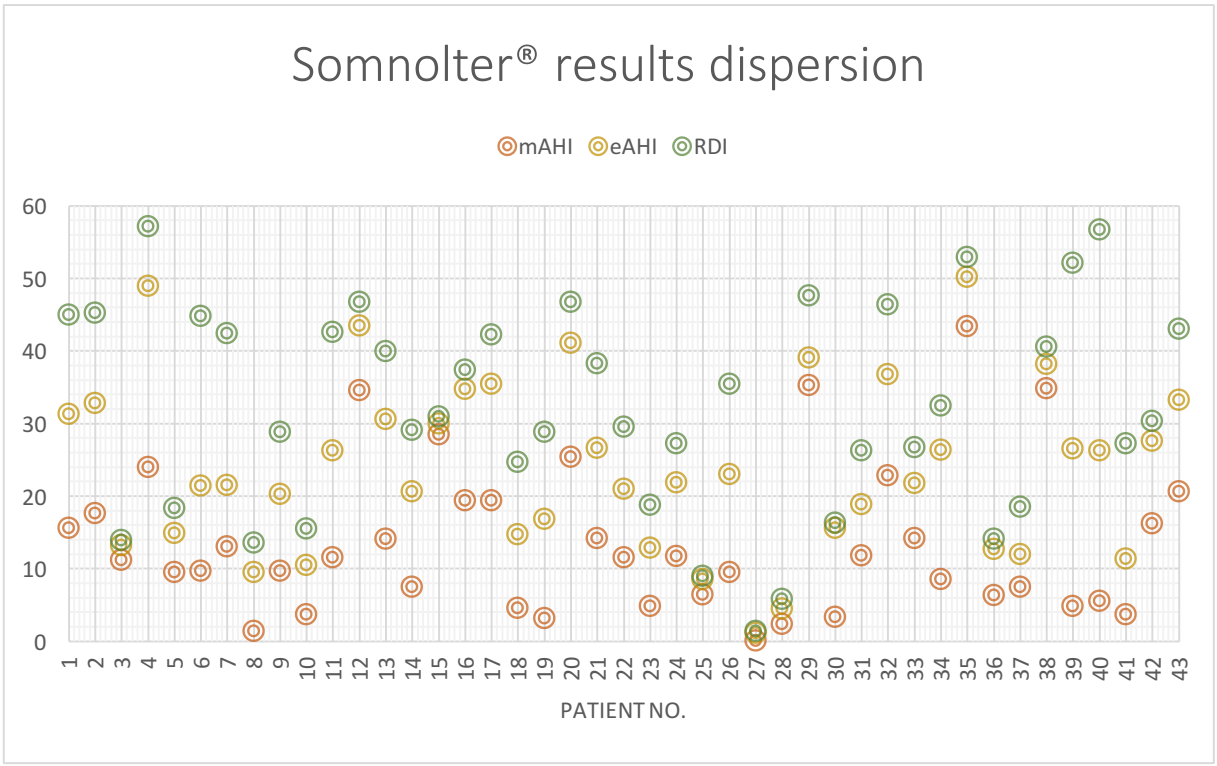
DISCUSSION

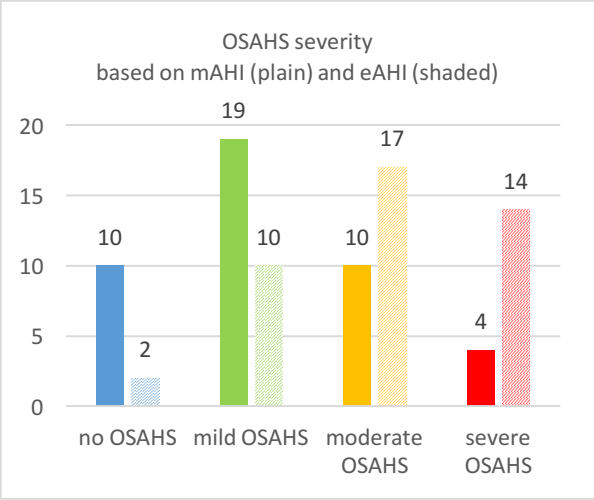
Prevalence and risk factors

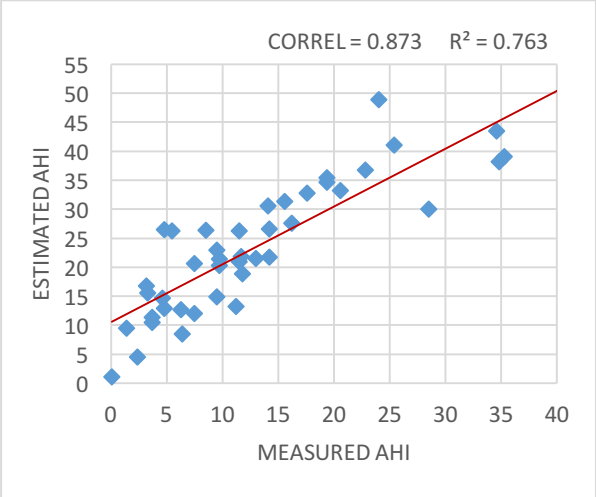
This study confirms the high prevalence of OSAHS in the heart failure population. We found a prevalence of 76.74% for all classes of OSAHS and 30.23% for the moderate to severe group.

The latter is the most conservative estimation of the OSAHS prevalence we found, yet it is still significantly higher than the prevalence in the general population, which is estimated towards 4% in men and 2% in women. The prevalence numbers we found are in correspondence with previous research reporting an OSAHS prevalence rising to 50% in certain cardiovascular diseases (*vide supra*).

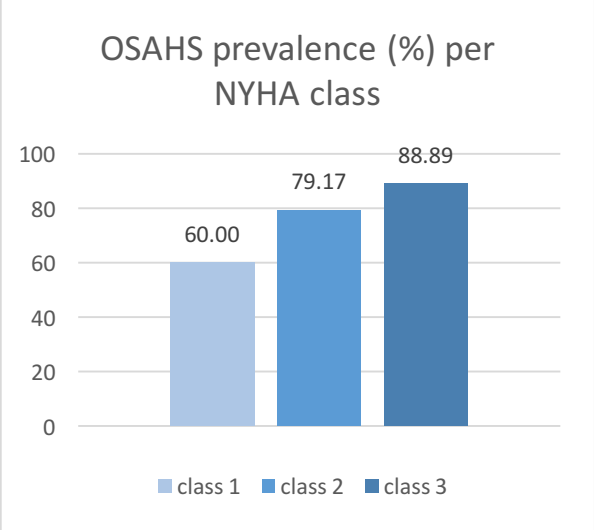
Because of the technical properties of the home monitoring device, which does not contain an EEG, we must reckon with a certain margin of uncertainty in the interpretation, since only the hypopnoeas with desaturation can be measured, while the hypopnoeas with micro-arousals are estimated through indirect parameters. In our study, the divergence between the mAHI and the eAHI varies from 1.0 to 24.9, with a mean difference of 10.50 ± 1.70, which is substantial. It is probable that the more pronounced the difference between the mAHI and the eAHI, the higher the likelihood of underestimation and overestimation using one of these values, respectively. The dispersion table below gives a visual overview of the divergence of the results per patient. Because of this divergence, a shift towards the moderate and severe OSAHS classes was seen when we based the classification on the estimated AHI, reducing the numbers of negatives and mild cases of OSAHS. This right-shift is illustrated in the graph below. Making use of the eAHI rather than the mAHI, likely enhances specificity, at the expense of sensitivity. Further research into this subject seems warranted. The correlation between both values is very strong, as would be expected (correlation coefficient 0.873).

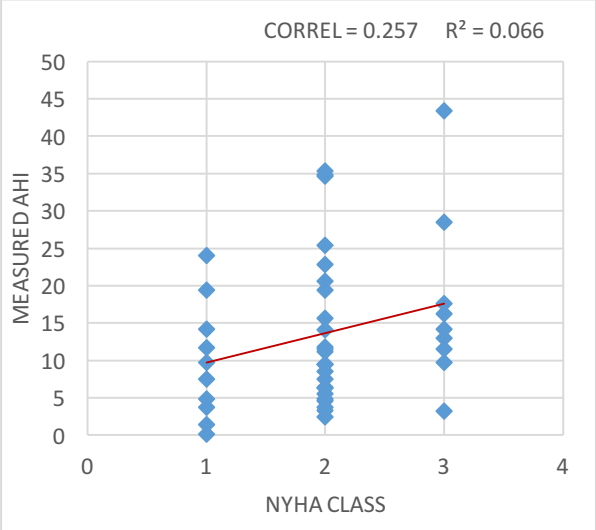




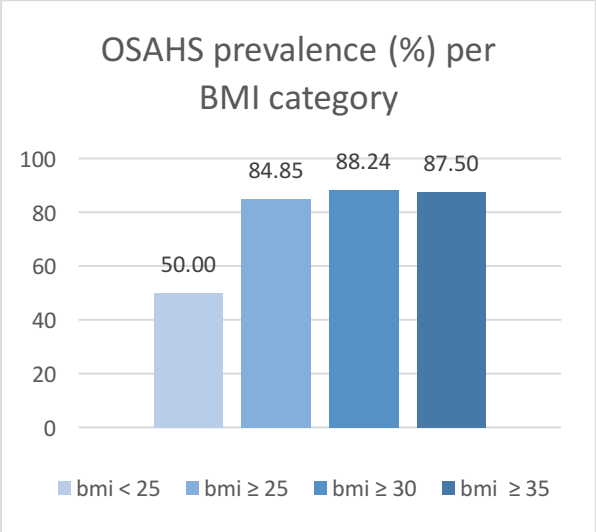


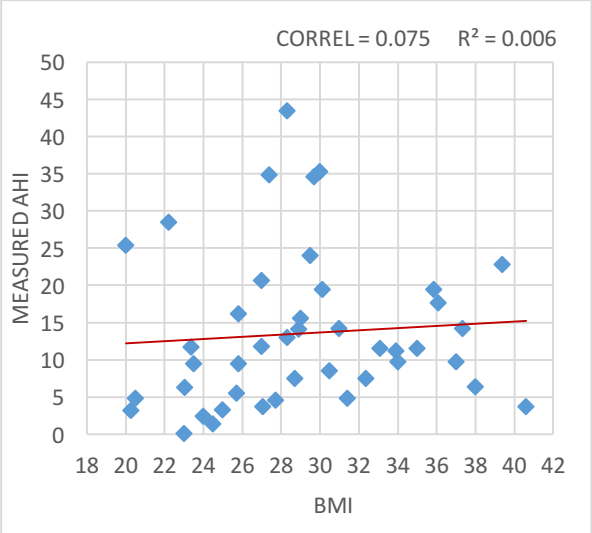
The prevalence of OSAHS was higher in the higher NYHA classes; in class 1 the prevalence was 60.00%, in class 2 this rose to 79.17% and the highest prevalence was seen in class 3 with 88.89%. We found a weak correlation between the NYHA class and the OSAHS severity index (correlation coefficient 0.257 and $R^2 = 0.066$).

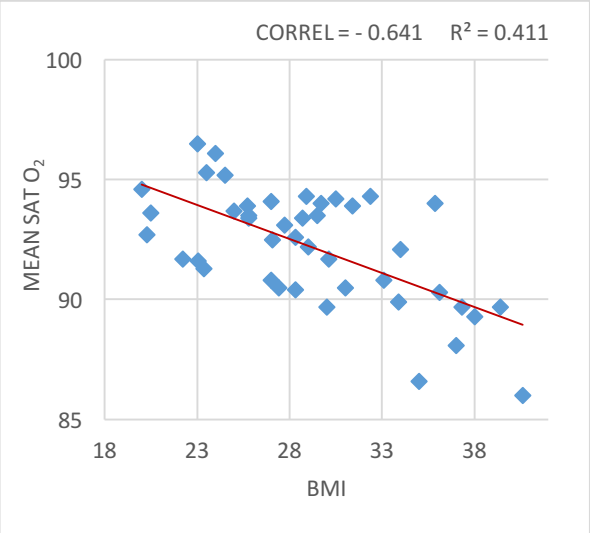




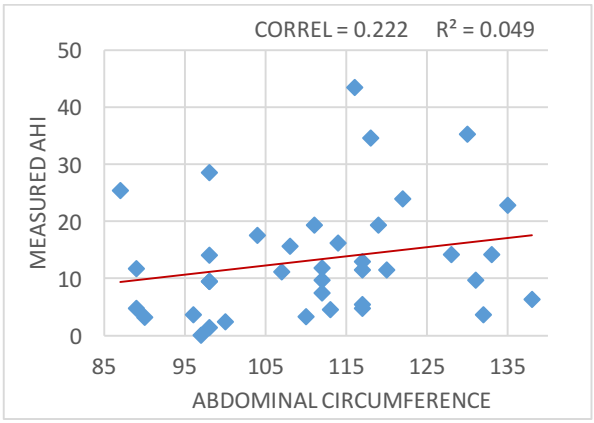
In the patient group with a body mass index under 25, we found an OSAHS prevalence of 50%. This was considerably lower than the over 80% prevalence rates in the patients with a higher BMI, thus supporting the theory that obesity is an important risk factor for OSAHS. However, no correlation was found between BMI and the mAHI (correlation coefficient = 0.075). Even so, there was a strong correlation between the mean oxygen saturation and BMI.

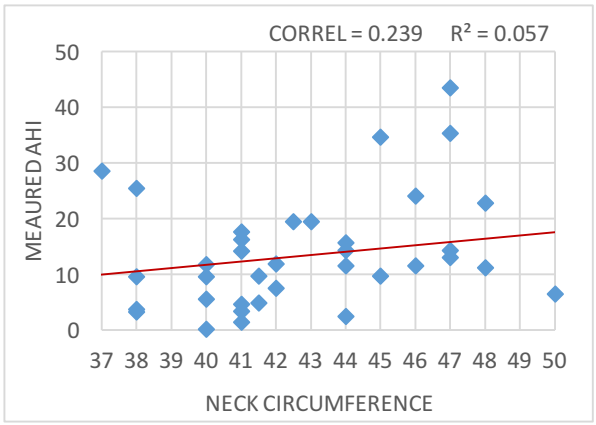


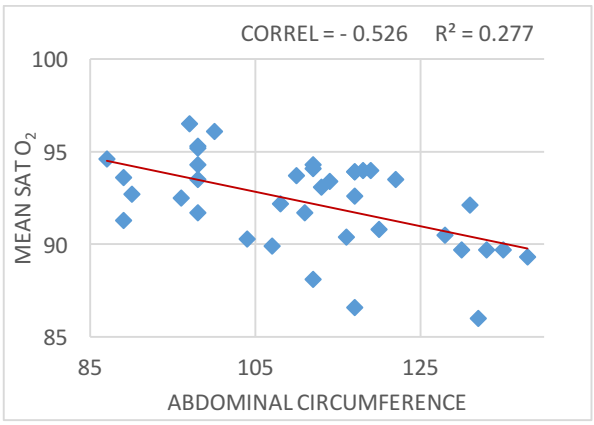


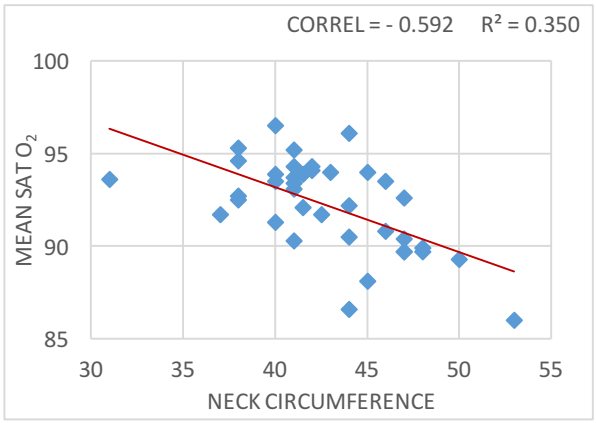


The correlations between the AHI and the abdominal and neck circumference were weak and in the order of magnitude of the correlation between the AHI and the NYHA class. The correlation coefficients were 0.222 and 0.239, respectively. There was however a strong correlation with the mean oxygen saturation. The correlation coefficients were -0.526 for the abdominal and -0.592 for the neck circumference.









The prevalence in men was equal to that in women; 76.47% vs. 77.78%, respectively, for mild to severe OSAHS and 32.35% vs. 33.33% for moderate to severe OSAHS. Yet mind that the number of female participants was significantly smaller with a male-to-female ratio of 3.77.

Questionnaires

The impact on the quality of life assessed by questionnaires seems to be rather limited. However, it is clear that patients tend to overestimate their quality of sleep, as is demonstrated by the poor predictive values and the weak or non-existent correlation between the questionnaires and the Somnolter® results, as we shall see here. This study confirms that because of this error of judgement, questionnaires are unreliable to screen for OSAHS in the heart failure population. We discuss the separate questionnaires below.

STOP-BANG Questionnaire

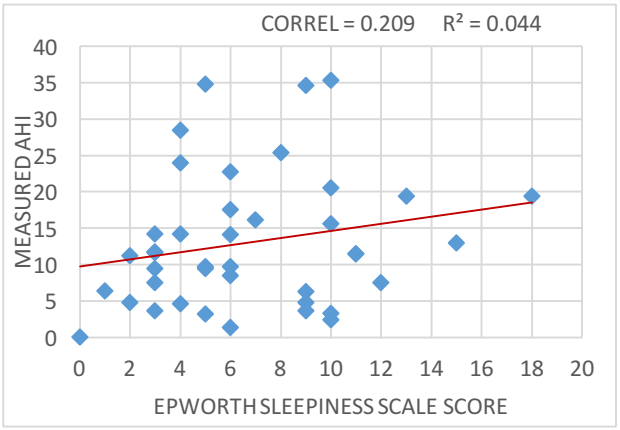
The STOP-BANG questionnaire is for a substantial part composed of objective parameters known to be risk factors for OSAHS (BMI, neck circumference, age and gender). Therefore, it is less susceptible to interpretation variability. However, most of these parameters tend to be

present in the chronic heart failure population and the cut-off value of ≥ 3 was reached by all patients. We therefore endorse the use of the ≥ 5 criterium, as has already been suggested in other publications (supra). Using this value, we found a sensitivity of 68.75%, still paired with a very low specificity of 36.36%. These results are in line with previous research on the STOP-BANG questionnaire. There was no correlation between the score and the mAHI (correlation coefficient = 0.116).

Berlin Questionnaire

For the Berlin questionnaire, we found a sensitivity of 67.65%. This is quite similar to the STOP-BANG's, but the lower number of false positives results in a better specificity of 66.67%. Nevertheless, these values are far from ideal and significantly lower than the predictive values that are reported in the overall population. Patients are divided in a low risk and high risk group and no quantitative score is given.

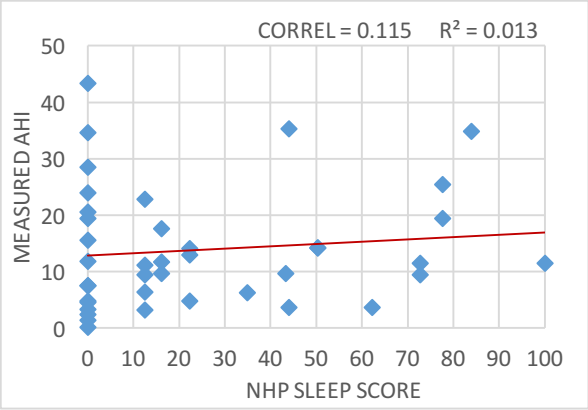
Epworth Sleepiness Scale

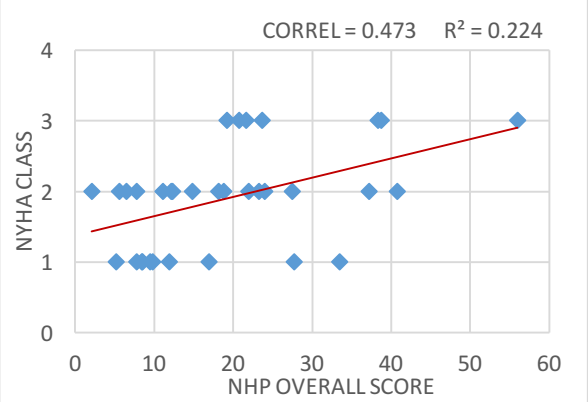


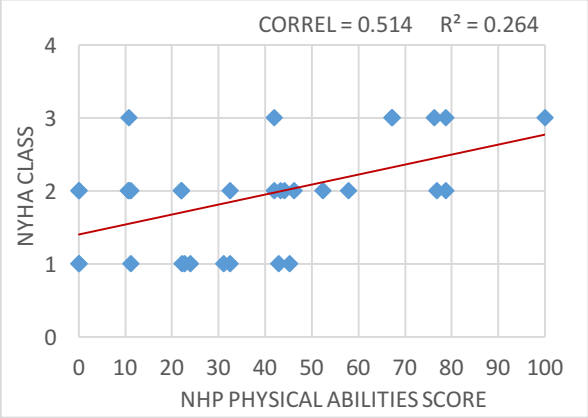
Remarkable is the fact that the Epworth Sleepiness Scale had very poor sensitivity in detecting OSAHS in our study, despite its being widely used in the OSAHS work-up and therapy evaluation. When using the ESS > 7 cut-off value, we found a sensitivity of a mere 36.36% with a specificity of 60.00%. The correlation between the Epworth score and the measured AHI was weak, leaning to very weak, with a correlation coefficient of 0.209 with $R^2 = 0.044$ for a mean ESS score of 6.73 (± 1.21). We would argue that this effect might be due to the characteristics of the heart failure population, where the mean age is high and activity levels tend to be low. For this reason, we think that questions 3, 4 and 8 of the ESS concern situations and activities that are often not applicable to these patients, thus automatically resulting in a negative answer, without actually assessing the chance of falling asleep. These questions propose the following scenarios: *"Sitting, inactive in a public place (e.g. a theatre or a meeting)"*, *"As a passenger in a car for an hour without a break"* and *"In a car, while stopped for a few minutes in the traffic"*. The sensitivity we found was too low to embrace the ESS as a satisfactory screening tool for OSAHS in the chronic heart failure population. For the same reason, we deem it unlikely that it is useful for the follow-up of OSAHS treatment in heart failure patients.

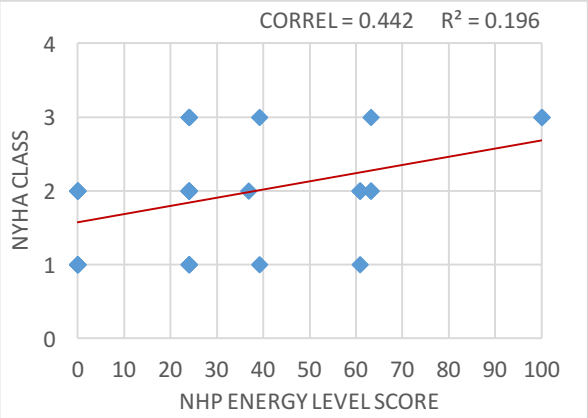
Nottingham Health Profile

The Nottingham Health Profile had a mean score of 20.02 (± 3.92) on a maximum of 100. The most affected domains are *physical ability* and *energy level* with a mean score of 36.31 (± 7.92) and 31.82 (± 9.18), respectively. The *sleep* domain came in third place with a mean score of 24.81 (± 9.16). There is a moderate correlation between the *physical ability* and *energy level* scores and the NYHA class, where there is no correlation between the *sleep* score and the measured AHI (correlation coefficient = 0.115). It is noteworthy that 40% of all patients scored the *sleep* domain with 0, indicating that they experienced no sleeping problems, while 62.50% of them did indeed have mild to severe OSAHS. This suggests that the symptoms of chronic heart failure are perceived as more debilitating by the patients, while the sleep quality is either overestimated, or not interfering with daily activity. After all, the NHP is designed to only detect moderate to severe problems, in order to avoid a high number of false positives. Then again, daytime somnolence caused by OSAHS might interfere with or reflected in the questions from the other domains, but there was no evident correlation with the mAHI. Therefore, we refrain from conclusions concerning this matter.



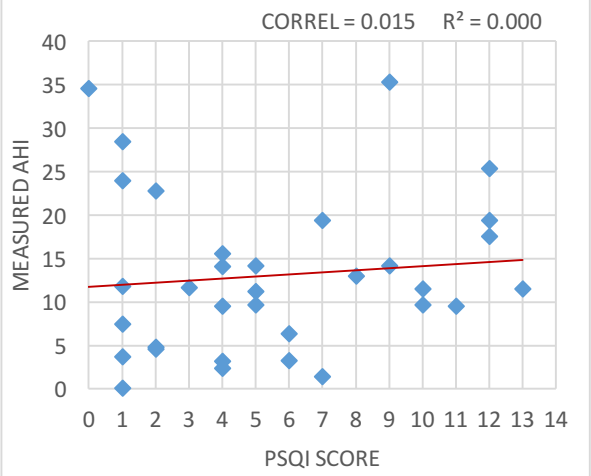






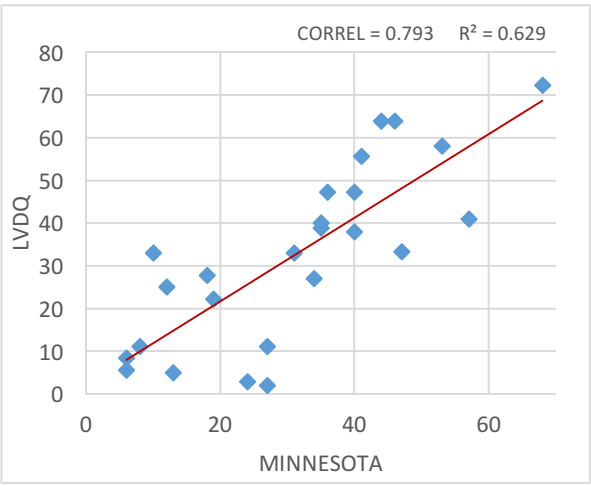
Pittsburgh Sleep Quality Index

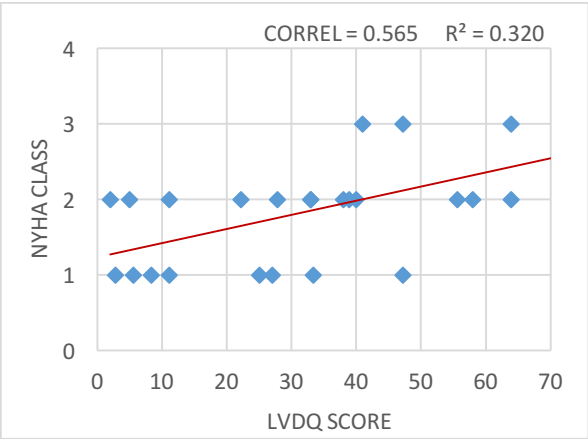
The Pittsburgh Sleep Quality Index had a sensitivity of 60.61% in detecting mild to severe OSAHS at a cut-off value of 5, with a specificity of 60.00%. Given that it is not specifically designed for the detection of OSAHS, it showed relatively good predictive values compared to the specific sleep apnoea questionnaires. Nonetheless, we found no correlation between the PSQI score and the mAHI (correlation coefficient = 0.015).

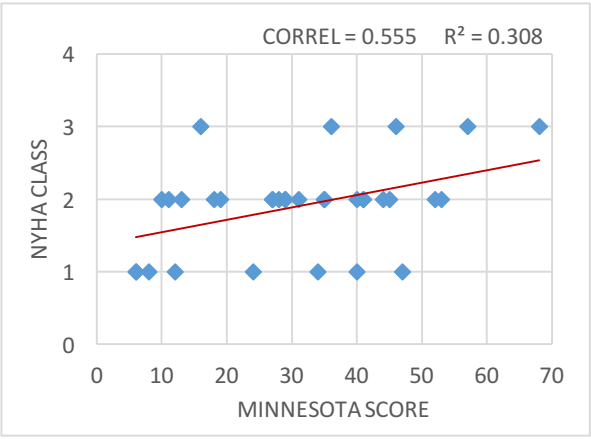


Chronic heart failure questionnaires

Next to the OSAHS and sleep quality questionnaires, we plotted the scores of the Left Ventricular Dysfunction Questionnaire and Minnesota Living With Heart Failure Questionnaire in function of the NYHA class. We found a moderate, leaning towards strong, correlation with a coefficient of 0.565 and 0.555, respectively. Both questionnaires had a strong, bordering on very strong, mutual correlation of 0.793 with $R^2 = 0.629$.







We conclude that questionnaires are per se prone to a significant self-report bias and a limitation in the analysis, is the length of our survey set, which contained 7 questionnaires. The

long time that was needed to fill in these questionnaires (25 to 35 minutes) undoubtedly interfered with patients' motivation and accuracy in the completion of the entire list, thereby possibly increasing the self-report bias.

On the other hand, some specific questions proved to be difficult to answer on themselves, which is an effect that would also occur when single questionnaires are used. This mainly occurred with questions that were not relatable for the patient (notably in the ESS, *vide supra*) and questions that asked to estimate quantitative parameters like sleep duration, sleep latency, etc. (especially the PSQI). This raises doubts about the accuracy of the answers and could, at least partially, explain the poor correlation between reported and measured sleep quality. While this effect might be compensated by incorporating objective parameters that are known risk factors for OSAHS (for instance age, sex, abdominal and neck circumference, obesity, hypertension), these were present in most patients, thereby rendering the questionnaires useless because of a lack of specificity. This effect was most distinct in the STOP-BANG questionnaire. Although night time symptoms of chronic heart failure can have an effect on the results of sleep quality questionnaires, thereby influencing their predictive values, the effect of the aforementioned inaccuracy is perhaps equally as important and not limited to the chronic heart failure population.

In contrast, the chronic heart failure questionnaires are indeed capable of making a reliable assessment of the perceived health status that correlates well with the NYHA class. This is an argument for a systematic underestimation of the OSAHS prevalence when making use of the specific sleep questionnaires that is inherent rather to the questionnaires, than to the patient's ability to answer them in accordance with his perception. As we already discussed, we believe that this is partially because of the unclear distinction between sleep apnoea induced somnolence and heart failure induced fatigue, and partially because of the inadequacy of some questions in the chronic heart failure population.

LIMITATIONS

The authors acknowledge a few limitations of this study:

We used an ambulatory sleep monitor device to screen for obstructive sleep apnoea disorder. Although it has proven to be a promising instrument with high specificity and sensitivity, it is not the gold standard for OSAHS diagnosis.

Questionnaires are prone to significant differences in interpersonal interpretation and are susceptible to momentary alterations in the patient's perception. Our patients were asked to

complete seven questionnaires, which, at least for some of them, has proven to be a demanding task. It is unclear if, and to which extent, this has interfered with their accuracy completing the questionnaires.

Two of the questionnaires we used (PSQI and LVDQ) had no validated Dutch version, so we used an unvalidated translation.

The neck and abdominal measurements were performed by different researchers and are prone to variability, despite clear instructions.

A possible selection may have occurred if patients who experienced sleeping problems were more motivated to participate. Inversely, one patient who met all inclusion criteria was already being treated with CPAP and preferred not to participate in order not to compromise his sleep quality.

CONCLUSION

Using an ambulatory sleep monitor, we found a high prevalence of OSAHS in the chronic heart failure population, with the most conservative estimation of 32.56%, being significantly higher than the estimated overall prevalence of 2 to 4%. We found that the higher the NYHA class, the higher the prevalence of OSAHS and there was a weak correlation between the NYHA class and the measured AHI.

Next to this, we demonstrated that questionnaires are not a good instrument to screen for OSAHS in the heart failure population, because of their low sensitivity and specificity in this patient population. Also, there was only a weak correlation between the sleep questionnaires and the AHI, while a moderate correlation between the heart failure questionnaires and NYHA class could indeed be demonstrated. Since ambulatory sleep monitoring has proven its practical feasibility, with higher combined sensitivity and specificity next to the questionnaires, we cannot recommend questionnaires as a screening tool for OSAHS in the population with chronic heart failure and would rather endorse the immediate use of home monitoring, which can easily be accomplished in a primary care setting.

Still, it is important to emphasise the difference between the use of questionnaires as screening tools and their use as markers in follow-up. While we conclude that the sensitivity of the OSAHS questionnaires is too low to support their use as screening instruments, we cannot make conclusions about their use in follow-up during OSAHS treatment in the chronic heart failure population. This question might be addressed in a future observational study that

evaluates the impact of mandibular adjustment devices or CPAP treatment on the quality of life.

At this point, we can draw no conclusion as to whether or not the high OSAHS prevalence is caused by chronic heart failure itself, or by the multitude of risk factors that are inherent to this patient population. We would nonetheless like to argue that for clinical practice, it is not essential to know if there is a direct causal relationship between OSAHS and heart failure. More important is the awareness of the high prevalence of OSAHS in the heart failure population and the notion that early detection and treatment of sleep apnoea disorders can significantly reduce cardiovascular mortality, as previous studies have demonstrated. In this perspective we do recommend a high level of alertness for physicians to identify OSAHS in chronic heart failure patients as early as possible and we believe to have found arguments to endorse a systematic screening for sleep-related breathing disorders in this specific population. A prospective study to establish the effects of MAD and CPAP treatment on the progression of chronic heart failure seems opportune.

Appendix 1: Study protocol (definitive version 170118)

ARE SLEEP-RELATED BREATHING DISORDERS PART OF THE SYNDROME OF CHRONIC HEART FAILURE?

1. Inclusie- en exclusiecriteria

1.1. Inclusiecriteria

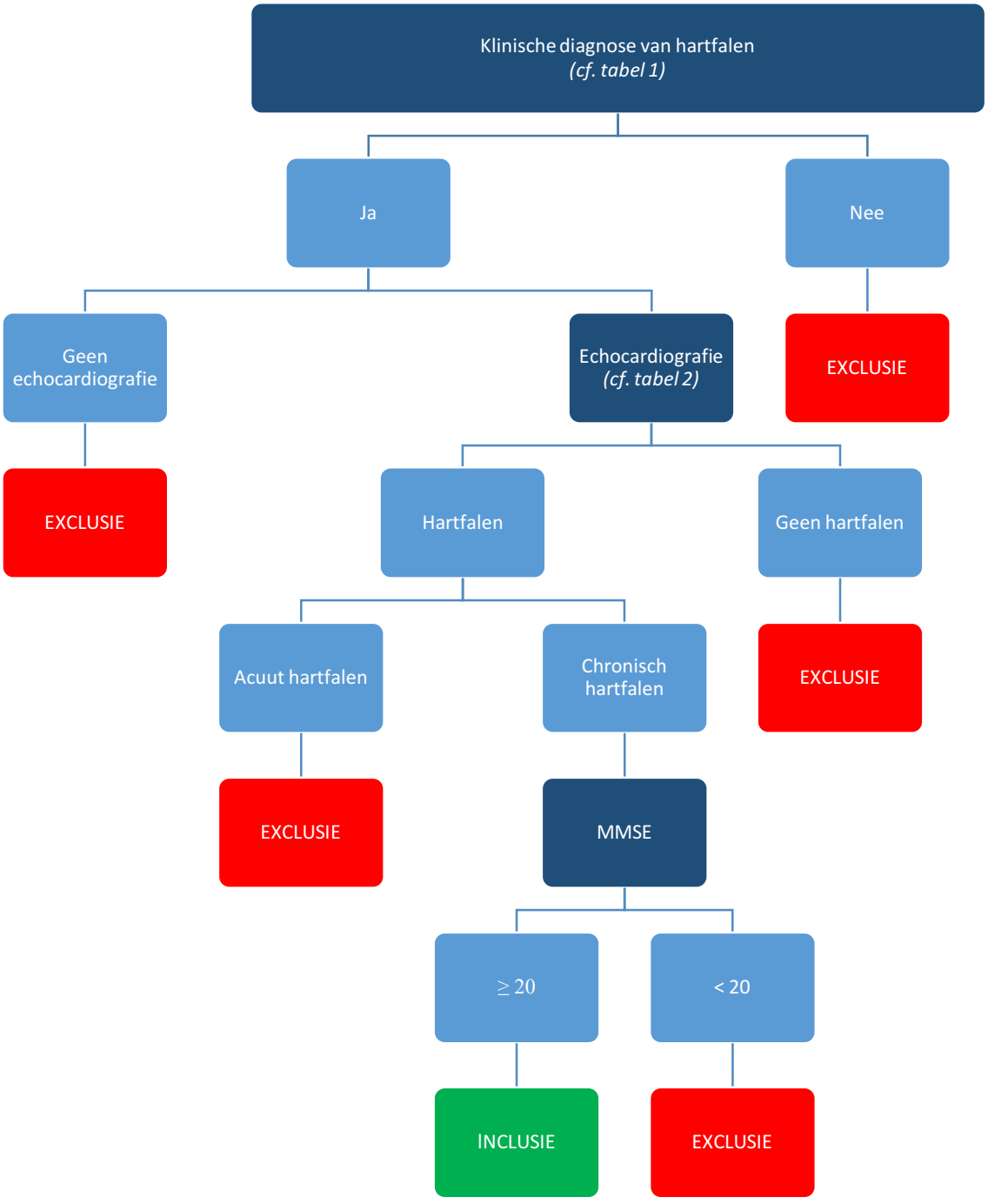
We includeren alle patiënten met een klinische diagnose van hartfalen EN bevestigde diagnose via echocardiografie.
We gebruikten de richtlijnen van de European Society of Cardiology om tot specifieke inclusiecriteria te komen. Deze worden weergegeven in de tabellen hieronder.
In tabel 1 staan tekens en symptomen van chronisch hartfalen, onderverdeeld in majeure en mineure criteria. De diagnose hartfalen vereist minstens **twee majeure criteria** of een **majeur criterium plus twee mineure criteria**.
We includeren alle patiënten waarbij via echocardiografie **minstens 1** van de bevindingen compatibel met hartfalen (cf. tabel 2) werd vastgesteld en waarmee de diagnose aldus werd bevestigd.

TABEL 1: KLINISCHE DIAGNOSE CHRONISCH HARTFALEN	
Majeure criteria	**Mineure criteria**
Paroxysmale nachtelijke dyspneu	Perifere oedemen
Orthopneu	Nachtelijke hoest
Verhoogde CVD	Dyspneu bij inspanning
3de harttoon / galopritme	Hepatomegalie
Cardiomegalie op RX thorax	Pleuravochtuitstorting
Longoedeem op RX thorax	Hartritme > 120 spm
	Gewichtsverlies > 4,5 kg op 5 dagen

TABEL 2: ECHOCARDIOGRAFISCHE BEVINDINGEN BIJ HARTFALEN	
Systolisch hartfalen	**Diastolisch hartfalen** (normale LVEF (≥ 50%) en geen LV dilatatie)
LVEF < 50%	Vertraagde diastolische relaxatie o.b.v: 1. e' gedaald (< 8 cm/s septaal of < 10 cm/s lateraal of < 9 cm/s gemiddeld) 2. E/A < 1
Einddiastolisch volume LV > 97 mL/m²	Verhoogde vullingsdruk o.b.v: 3. E/e' > 15 4. E/A > 2 5. Duur [A_{pulm}-A_{mitr}] > 30 ms
Eindsystolisch volume LV > 43 mL/m²	

1.2. Exclusiecriteria

- Cognitief deficit met MMSE < 20.
- Patiënten in fase van acuut hartfalen.
- Patiënten met een acute respiratoire infectie.



1.3. Rekrutering

We rekruteren alle patiënten in huisartsenpraktijken die omwille van een klinisch beeld van hartfalen een echocardiografisch onderzoek ondergingen waarbij hartfalen werd bevestigd volgens de bovengenoemde criteria.

2. Achtergrondvariabelen en questionnaires

2.1. Achtergrondvariabelen

Dossiergegevens	**Anamnestische gegevens**	**Meetwaarden**
Cardiovasculaire status	Rookgedrag	BMI
Diabetes	Alcoholgebruik	Buikomtrek
COPD / astma	Snurkgedrag	Nekomtrek
Aangeboren syndromen (bv. Palatoschisis) en allergieën	Familiaal voorkomen OSAHS	Antwoorden questionnaires (De patiënt worden de 7 hieronder vernoemde vragenlijsten voorgelegd.)
Heelkundige voorgeschiedenis		
Medicatie		

2.2. Questionnaires

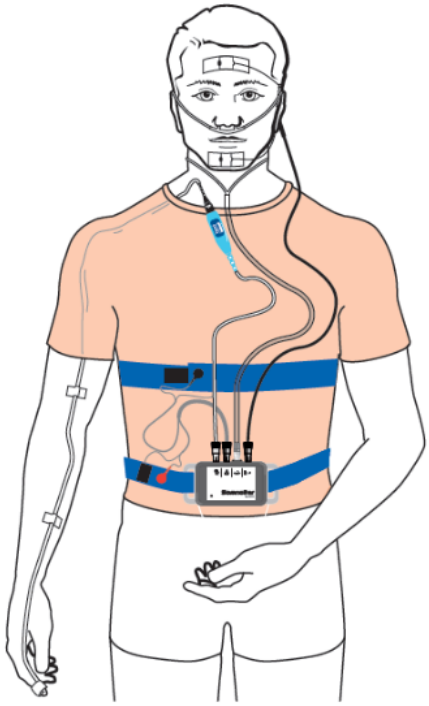
We scoren de patiënt door middel van 7 vragenlijsten op domeinen die beïnvloed kunnen zijn door de slaap (*Prog Respir Res. Basel, Karger, 2006, vol 35, pp 37-42*). Daarbij wordt eerst breed gepeild naar de levenskwaliteit, waarna specifiek de slaapkwaliteit, slaperigheidsklachten en ten slotte de specifieke symptomen van OSAHS worden bevraagd. Daarnaast maken we een inschatting van de klinische implicaties van het hartfalen via 2 domeinspecifieke questionnaires. De selectie van de vragenlijsten gebeurt op basis van hun validering in de gevonden literatuur betreffende hun specifieke deeldomeinen. We weerhielden:

- Epworth Sleepiness Scale
- STOP-Bang Questionnaire
- Pittsburgh Sleep Quality Index
- Nottingham Health Profile
- Berlin Questionnaire
- Minnesota Living with Heart Failure Questionnaire
- Left Ventricular Dysfunction Questionnaire

We correleren de scores later met de uitslagen van het slaaponderzoek om de waarde als screeningsmethode in de praktijk te kunnen inschatten. Via Bayesiaanse analyse wordt de waarde van de questionnaires ingeschat, vervolgens wordt gezocht naar een verband met de achtergrondvariabelen op basis van een regressie-analyse.

3. Thuismonitoring

We gebruiken het Nomics Somnolter® toestel om bij de patiënt thuis een slaapregistratie op te nemen. Het toestel wordt ’s avonds bij de patiënt thuis bevestigd door één van de onderzoekers en ’s ochtends weer opgehaald. We vragen de slaapkwaliteit te scoren op een VAS-schaal en peilen naar ervaren ongemakken ten gevolge van het toestel. Patiënten bij wie de registratie is mislukt (te korte slaapduur, batterijproblemen, losgekomen sensoren, …), worden gevraagd een tweede nacht met het toestel te slapen.



De slaapregistratie wordt softwarematig verwerkt en de gemeten apneu/hypopneu index en respiratory disturbance index worden vergeleken met de resultaten van de vragenlijsten. We berekenen de prevalentie en zoeken naar correlatie met de variabelen en de questionnaires via regressie-analyse.

4. Follow-up

De resultaten worden overgemaakt aan de patiënt en de behandelende arts, die verzocht wordt om in samenspraak met de patiënt een eventueel verder beleid (levensstijladvies, polysomnografie, CPAP, …) uit te stippelen.

Appendix 2: ethical commission approval

Betreft uw aanvraag Ethische begeleiding masterproeven met titel "Are sleep-related breathing disorders part of the syndrome of chronic heart failure?" (mp19114)

Martine Goossens <martine.goossens@kuleuven.be>

wo 22/03/2017 19:28

Aan:Alec Smets <alexander.smets1@student.kuleuven.be>; Jean-Marie Degryse <jan.degryse@kuleuven.be>;

CC:Steven Dekeye <steven.dekeye@student.kuleuven.be>;

English version below

Geachte Heer/Mevrouw

De Opleidingspecifieke Ethische Begeleidingscommissie van de opleiding "Master in de huisartsgeneeskunde (Leuven e.a.)" heeft uw voorstel tot Masterproef "Are sleep-related breathing disorders part of the syndrome of chronic heart failure?" onderzocht en gunstig geadviseerd. Dit betekent dat de commissie van oordeel is dat de studie, zoals beschreven in het protocol, wetenschappelijk relevant en ethisch verantwoord is. Dit gunstig advies van de commissie houdt niet in dat zij de verantwoordelijkheid voor de geplande studie op zich neemt. U blijft hiervoor zelf verantwoordelijk. Indien u van plan bent uw masterproef te publiceren kan deze e-mail dienen als bewijs van goedkeuring.

Dear Mr/Ms

The Supervisory Committee on Medical ethics of the "Master in de huisartsgeneeskunde (Leuven e.a.)" programme has reviewed your master's thesis project proposal "Are sleep-related breathing disorders part of the syndrome of chronic heart failure?" and advises in its favour. This means that the committee has acknowledged that your project, as described in the protocol, is scientifically relevant and in line with prevailing ethical standards. This favourable advice does not entail the committee's responsibility for the planned project, however. You remain solely responsible. If you intend to publish your master's thesis, this e-mail may be used as proof of the committee's consent.

> De OBC keurt de aanvraag goed, maar wenst graag nog een antwoord op volgende vragen/suggesties: - wie doet wat? - in het IC wordt ook best volgende opgenomen: vrijheid van deelname, mogelijkheid terugtrekking studie, iets zeggen over vertrouwelijkheid van gegevens

Met vriendelijke groeten

Opleidingsspecifieke begeleidingscommissie van de opleiding Master in de huisartsgeneeskunde (Leuven e.a.)

Appendix 3: information and informed consent

KU Leuven
Faculteit Geneeskunde
Academisch Centrum Huisartsgeneeskunde
Kapucijnenvoer 33, blok J, PB 7001
3000 Leuven

OSAHS bij hartfalen: prevalentie en screening in de eerste lijn

informatie + informed Consent

Momenteel loopt aan de KU Leuven een onderzoek naar de relatie tussen een verminderde hartfunctie en slaapapneu. Onze praktijk werkt mee aan deze studie en op basis van uw medische voorgeschiedenis, hebben we vastgesteld dat u in aanmerking komt om aan het onderzoek deel te nemen. Hieronder vindt u meer informatie hieromtrent. Uiteraard moet u niet meteen beslissen of u al dan niet deelneemt; indien u nog vragen hebt, kan u hierover steeds met ons contact opnemen voor nadere informatie.

Wat is slaapapneu?

Slaapapneu is een slaapstoornis waarbij gedurende de slaap periodes van verzwakte ademhaling of kortstondige ademhalingsstilstand voorkomen. In veel gevallen treedt slaapapneu ongemerkt op en veel mensen beseffen niet dat ze korte adempauzes doormaken tijdens de slaap. Mogelijke symptomen van slaapapneu zijn snurken, plots wakker schrikken, vermoeidheidsklachten overdag (slaperigheid, concentratiestoornissen, prikkelbaarheid) en verhoogde bloeddruk.

Wat is het doel van deze studie?

Verscheidene studies suggereren dat slaapapneu frequenter voorkomt bij mensen met een verminderde hartfunctie, maar dat de aandoening omwille van de aspecifieke klachten vaak onopgemerkt blijft. Bovendien is vastgesteld dat slaapapneu kan gepaard gaan met een verhoogd risico op hart- en vaatziekten, zoals hoge bloeddruk en hartritmestoornissen. Om deze reden kan het belangrijk zijn om slaapapneu tijdig op te sporen. We willen nagaan of vragenlijsten over de slaapkwaliteit en een slaaponderzoek met een thuisregistratietoestel goede screeningsmethodes zijn om slaapapneu op te sporen.

Hoe ziet het onderzoek eruit?

Indien u beslist om deel te nemen aan het onderzoek, zal u uitgenodigd worden tot het invullen van een aantal vragenlijsten met betrekking tot de slaapkwaliteit. We zullen u ook enkele vragen stellen omtrent eventueel doorgemaakte ziektes, medicatiegebruik en rookgedrag.

Vervolgens zal uw slaappatroon gedurende één nacht bij u thuis worden gemeten door een Somnolter-toestel. Dit is een klein apparaatje dat de beweging van de kaak, borst en buik registreert en het zuurstofgehalte in het bloed en de hartslag meet.

Alle onderzoeken in deze studie zijn niet-invasief en pijnloos. Er zijn tevens geen risico's of neveneffecten aan verbonden. De resultaten van de registraties worden volledig anoniem verwerkt. Het studieontwerp werd voorgelegd aan en goedgekeurd door de Ethische Commissie van de KU Leuven. Voor deelname aan de studie is geen vergoeding voorzien. Conform de Belgische wet van 7 mei 2004 inzake experimenten op de menselijke persoon, is de opdrachtgever, zelfs foutloos, aansprakelijk voor alle schade die de deelnemer of zijn rechthebbenden opliepen en die rechtstreeks dan wel onrechtstreeks verband vertoont met het experiment. De opdrachtgever van deze studie (KU Leuven) heeft een verzekering afgesloten die deze aansprakelijkheid dekt. Indien u schade zou oplopen ten gevolge van uw deelname aan deze studie zal die schade bijgevolg worden vergoed conform de Belgische wet van 7 mei 2004.

Het verloop van de studie

Het invullen van de vragenlijsten zal ongeveer 30 minuten van uw tijd vragen.

De registratie met Somnolter gebeurt volledig bij u thuis; een medewerker van de studie zal het toestel 's avonds komen aanbrengen en vervolgens kan u gewoon gaan slapen. De volgende dag wordt het toestel bij u thuis opgehaald.

We nemen na een drietal dagen telefonisch contact met u op om de resultaten van de studie kort te overlopen. Het verslag van uw slaaponderzoek kan ook worden toegevoegd aan uw globaal medisch dossier.

De kosten van de slaapstudie worden volledig gedekt door de KU Leuven. Bijgevolg is dit onderzoek voor u volledig gratis.

Steeds bereid tot nadere informatie,

dr. Steven Dekeye - dr. Stijn Boenders - dr. Silke De Cleyn - prof. dr. Jan Degryse

INFORMED CONSENT

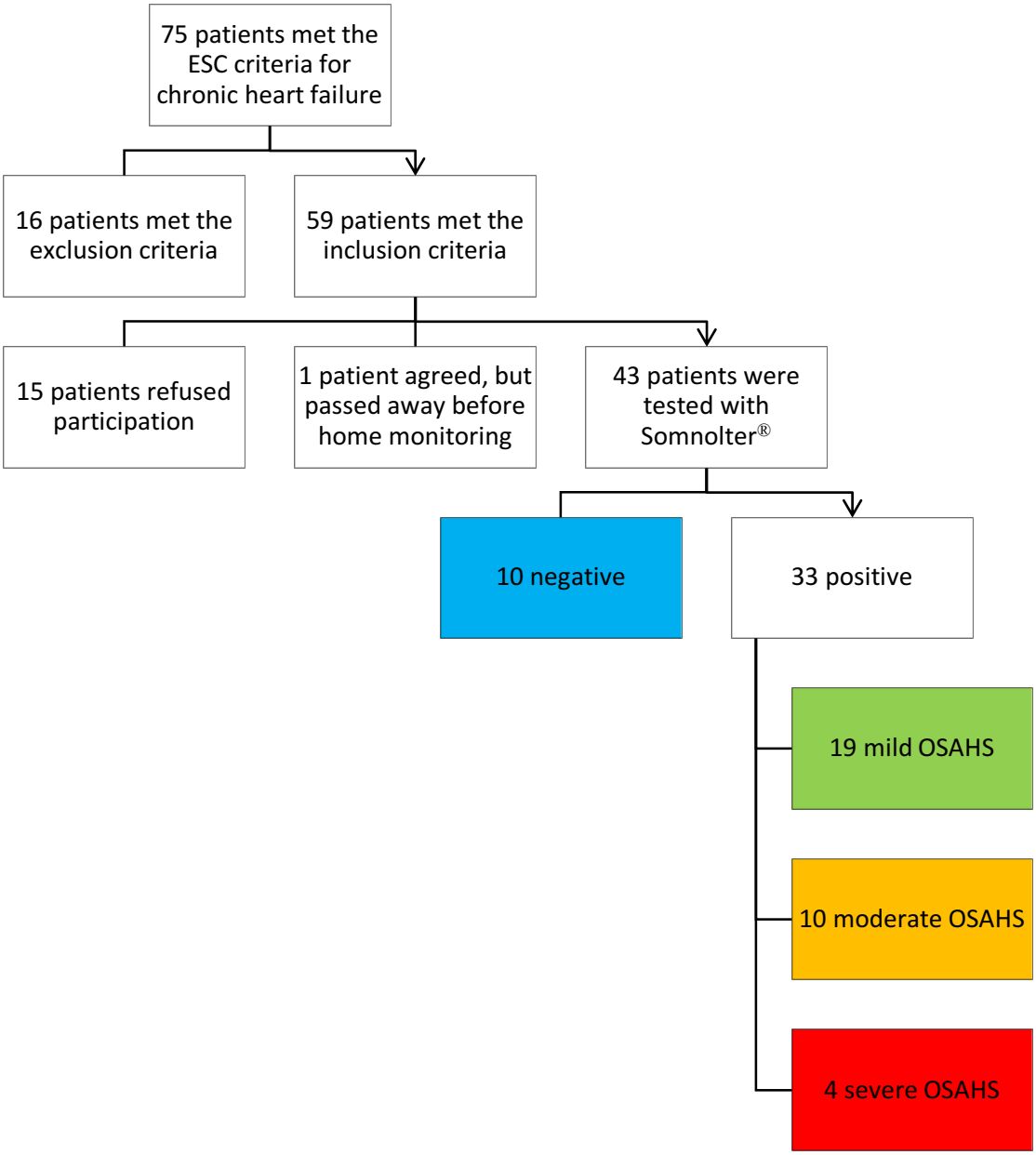
Ik heb kennis genomen van de bovenstaande informatie en heb de kans gehad om mij hierover voldoende te informeren. Ik stem vrijwillig toe om deel te nemen aan deze studie en begrijp dat ik het recht heb om elk onderzoek te weigeren en op eender welk moment mijn deelname aan de studie stop te zetten.

Naam en voornaam: _____

Datum: ____ / ____ / _____

Handtekening:

Appendix 4: Algorithm



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