The occurrence of arrhythmias during daily living

The relationship between daily activities and premature beats

Master thesis

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SAMENVATTING

Achtergrond informatie

Een aritmie is een hartaandoening die enkele miljoenen patiënten wereldwijd treft. Lichaamsbeweging is van groot belang om nadelige gezondheidseffecten van hartpatiënten te beperken. Echter, goedaardige hartritmestoornissen zoals premature hartslagen worden vaak ervaren door patiënten, wat een negatieve impact kan hebben op de psychologische keuzes in het dagelijks leven. Patiënten kunnen meer sedentair worden en zich richten op licht intensieve activiteiten om de symptomen als gevolg van premature hartslagen te vermijden.

Doelstelling

Het onderzoeken van de relatie tussen dagelijkse activiteiten (wandelen en fietsen) en het optreden van premature hartslagen in patiënten die een Holter onderzoek ondergaan. Het secundaire doel van deze studie was het onderzoeken van de relatie tussen tijd van de dag, patiënt karakteristieken, medicijn inname en premature hartslagen.

Methode

Patiënten (n=16) kregen een Holter recorder, met daarbij een fotoplethysmografie en accelerometer gebaseerde polssensor. Het onderzoek bestond uit een thuis monitoring periode. De exacte tekentoets, Mann-Whitney U test en Spearman rangorde correlatie tests zijn gebruikt om significante verbanden te onderzoeken.

Resultaten

Er is geen significant verschil gevonden tussen tijdens- en na activiteit. Ook is er geen significant verschil gevonden tussen premature hartslagen en tijd van de dag. De dichtheid van ventriculaire premature hartslagen tijdens wandelen en de totale dichtheid van premature hartslagen in de ochtend was significant hoger bij mannen dan bij vrouwen ($p=.020$, $p=.031$). Een toename van de Body Mass Index (BMI) werd geassocieerd met een toename van premature slagen tijdens de nacht ($p=.030$). Bovendien is er een trend gevonden naar een positieve correlatie tussen de leeftijd en supraventriculaire premature hartslagen tijdens het wandelen ($p=.073$). De kleine hoeveelheid patiënten met medicatie of co morbiditeit was te laag om conclusies te kunnen trekken.

Conclusie

Er is geen relatie gevonden tussen dagelijkse activiteit en het optreden van premature hartslagen. Echter, een belangrijke bevinding die overeenkomt met eerdere studieresultaten is het feit dat er een positieve relatie is gevonden tussen BMI, leeftijd en premature hartslagen.

Klinische relevantie

Vanwege de kleine studie populatie is aanvullend onderzoek nodig om de resultaten te kunnen bevestigen. Echter, er is geen belangrijke oorzaak-gevolg relatie tussen dagelijkse activiteiten

en premature hartslagen gevonden, waardoor het onwaarschijnlijk is dat dagelijkse activiteit aritmie-gerelateerde symptomen verhogen.

ABSTRACT

Background

An arrhythmia is a cardiac condition affecting several million patients worldwide. Exercise and physical activity participation is of paramount importance to mitigate risks for adverse health events in cardiac patients. However, benign arrhythmias like premature beats are often perceived by patients and these events may have a negative psychological impact on patients' lifestyle choices. Indeed, patients may increase the sedentary and resting time and engage in more light-intensity activities to avoid symptoms due to premature beats.

Aim

Investigate the relationship between daily activities (walking and cycling) and the occurrence of premature beats in patients suffering from cardiac symptoms. Second, investigate the relationship between time of the day, patient characteristics, medicine intake, and comorbidities and premature beats.

Methods

Patients (n=16) received a Holter recorder as part of usual care accompanied by a wrist worn photoplethysmography and accelerometer sensor. The study consisted of a home monitoring period. The exact sign test, Mann-Whitney U test, and Spearman's rank-order correlation tests were used to investigate significant relationships.

Results

No significant difference was found comparing during- and after activity. Furthermore, no significant difference was found for premature beats and time of the day. The density of ventricular premature beats during walking and the total density of premature beats in the morning was significantly higher in males compared to females ($p=.020$, $p=.031$). An increase in body mass index (BMI) was associated with an increase of premature beats during the night ($p=.030$). Furthermore, there was a trend towards a positive correlation between age and the density of supraventricular premature beats during walking ($p=.073$). The amount of patients having medication or comorbidities was not sufficiently large to draw any conclusions about the relationship to occurrence of premature beats.

Conclusion

No relation was found between daily activities and the occurrence of premature beats. However, an important finding is the positive relation between BMI, age and premature beats.

Clinical Relevance

Due the small study population, additional research needs to be performed to confirm the results. However, habitual physical activity may not have any significant cause-effect relationship with premature beat onset in patients and is therefore unlikely to increase arrhythmia-related symptoms.

Keywords: Arrhythmia, premature beats, activity, Supraventricular premature beats, Ventricular premature beats

INTRODUCTION

Cardiac arrhythmia is a condition in which the heart beats either irregular, too fast or too slow (1). The heart normally contracts when an electrical impulse from the sinoatrial (SA) node moves through the heart. In a healthy heart the pulsating beat is triggered by a synchronous electrical impulse (1). When the heart beat is disturbed, this is called an arrhythmia. There are several types of arrhythmias; irregular contraction of the atria, disorganized contractions of the ventricles, slow heart rate also called bradycardia, fast heart rate called tachycardia, atrial fibrillation (AF), conduction disorders, and several premature contractions of the heart (1).

Arrhythmias often occur in the elderly population or in patients who are having an hyperactive thyroid gland, a history of heart attack, cardiomyopathy, heart failures, heart operations, congenital heart disease or the use of alcohol, drugs or cigarettes (2). The exact prevalence of overall arrhythmia is unclear, but the estimated prevalence of the most common arrhythmia atrial fibrillation in the United States population is ranging from 0.1% among persons <55 years to 9.0% among patients of 80 years or older (3, 4). It is expected that with the aging population and better treatment options for myocardial infarction and heart failure, the incidence and prevalence will increase (3, 4) . The current prevalence for the Netherlands is still unknown.

Premature contractions of the heart are extra, abnormal heartbeats that can arise in both the atria and the ventricles. This abnormal beat disturbs the regular heart rhythm, sometimes causes a feeling of a flip-flop or skipped beat in the chest. Premature atrial contractions, also called supraventricular premature beats (SVPBs) have long been considered unlikely to result in serious clinical consequences (5). However, a study performed in 1998 demonstrated that treatment by targeted ablation of SVPBs among patients with Atrial Fibrillation, reduces arrhythmia recurrence (6). These findings strongly implicated SVPBs as an acute trigger for initiation among patients previously diagnosed with arrhythmia (5). Furthermore, excessive SVPBs are related to a higher risk of stroke. This growing evidence linking SVPBs to clinical disease suggest that SVPBs may represent a valuable clinical measurement that could change treatment paradigms (5).

Literature has shown that the proportion of ventricular premature beats (VPBs) increases in participants who start exercising (7, 8). Most of these studies were performed during controlled exercise on a treadmill. Results indicate that exercise revealed more serious rhythm abnormalities compared to inactive periods (8). Furthermore, research has indicated that isometric exercises are of more value than dynamic exercises when the aim is to unmask latent ventricular arrhythmias (9).

Recent investigation has suggested that VPBs during the recovery phase after exercise may be associated with a worse prognosis compared to VPBs during exercise (10). Long-term follow-up showed that both infrequent and frequent exercise related VPBs were associated with a 60% to 80% increase in risk of death from all causes (11). Not only during exercise, but also frequent or repetitive VPBs during routine activity in patients with known or suspected heart disease are

considered a marker for serious heart disease and a predictor for future cardiac events (12, 13). Literature also showed evidence that in some patients, the frequency of premature beats relate to the time of the day (14).

More and more, the attention has focused on the prognostic significance of ventricular premature beats developing during exercise (11). Several clinical studies have examined the association between ventricular premature beats and the risk of death in patients referred for diagnostic exercise testing. However, there are also studies that found no association, so results are still contradictory (10, 15-18).

A commonly used diagnostic tool in the first line of health care to detect arrhythmias is a Holter monitor (19). A Holter monitor is a portable, ambulatory electrocardiography (ECG) device which allows to monitor continuously various electrical activity of the cardiovascular system for 24 or 48 hours (19). However, it is proven that long-term monitoring has a superior diagnostic yield compared to a 24/48-hour Holter monitoring. However, the complexity of these devices are in some cases limited which lowers every-day clinical applicability (20). Key points for a monitoring device with a high sensitivity are long-term monitoring capabilities, simplicity, every-day use and a non-invasive nature (20). Recently, Philips Research (Wearable Sensing Technologies, WeST) developed a wrist worn photoplethysmography (PPG) and 3-axial accelerometer based sensor that complies with these demands. With this recently developed wrist worn device it could be helpful to measure the occurrence of arrhythmias during activities and in daily living with a higher sensitivity and non-invasively. Furthermore, new insights are needed to inform patients who have complaints by having premature beats, about what daily activities induce regarding the occurrence of premature beats. Additionally, exercise and physical activity participation is of paramount importance to mitigate risks for adverse health events and deterioration in cardiac patients. However, benign arrhythmias like SVPBs and VPBs are often perceived by patients and these events may have a psychological negative impact on patients' lifestyle choices. Indeed, patients may increase the sedentary and resting time and engage in more light-intensity activities to avoid symptoms due to premature beats especially when those are perceived during physical activity. Unravelling the link between occurrence of premature beats and daily life activities may help defining strategies to stimulate physical activity participation in patients suffering from palpitation symptoms and premature beats.

The current study is focussed on detecting ventricular- and supraventricular premature beats during- and after daily activities by using the wrist worn PPG sensor and the Holter monitor. The first aim of this study is to investigate the relationship between daily activities (walking and cycling) and the occurrence of premature beats in patients receiving a Holter recording for 24 or 48 hours. The secondary aim of this study is to investigate the relationship between time of the day, patient characteristics, medicine intake and comorbidities and premature beats.

METHODS

Participants and setting

The data used for this study is part of a larger study about arrhythmias and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement (STROBE). The intended objective of the complete study was to acquire PPG data with the wrist worn sensor in atrial fibrillation (AF) patients simultaneously with reference measurements. A cardiologist recruited a total of 23 patients. Patients were approached if diagnosed with AF or either were scheduled to undergo a Holter registration. Patients were excluded from the study either if the analyst reported fulltime AF (n=4) or flutter (n=2), or when patient had a comorbidity that kept the patient from normal daily activities (n=1). Finally, a total of 16 patients were included in the study. The study was performed at the Catharina Hospital of Eindhoven, the Netherlands and was approved by the Medical Ethics Committee of the Catharina hospital and the Internal Ethical Board (ICBE) of Philips Research. Patients willing to participate were asked to confirm eligibility and sign informed consent before participating in the study.

Data collection

All patients received a 24h or 48-hour Holter recording as part of usual care accompanied by the wrist worn PPG and 3-axial accelerometer (ACC) sensor on the non-dominant wrist. Thereafter, the electrodes were attached, the Holter recorder and the wrist worn sensor were set up and a diary was provided to the patients. A synchronization protocol was performed for later alignment of the two recordings and patients returned home to continue their usual daily activities. During this home monitoring period all patients were asked to keep track on their activities, complaints and medication intake by using the provided diary. After the 24 or 48 hours, patients returned the devices and diary. The Holter recordings were analysed by a specialized nurse, the PPG and ACC recordings were analysed by a Philips Research analyst.

Devices

The Holter recorder which was used in this study is the H12+ Holter recorder from the Mortara Instrument Inc. Manufacturer. This is a CE marked digital data logger for 12-lead ECG data. The wrist worn device that was used to measure heart rate and monitor activity was a CE marked, PPG and 3-axial accelerometer based data logger, developed by WeST, Philips Research. The provided diary was part of usual Holter monitoring procedure.

Outcome measures

Data provided by the Holter monitor used in standard clinical practice for arrhythmia and atrial fibrillation detection consists of ECG-derived interbeat intervals (IBIs) with relative classification of type of rhythm for each detected beat. Data by the diary was used to subtract the activity periods performed by the patient. Data provided by the wrist worn PPG sensor will consist of PPG and 3-axial acceleration data and will be processed for cardiac and motion features extraction. This data will be used to improve the activity classification from the diary.

Furthermore, patient- and procedure specific information was recorded including: i) demographic information (gender, age, weight, and height), ii) relevant clinical information (diagnosed medical conditions and medical prescription).

Daily activities (walking, cycling) and sleep periods were classified by a combination of patients reported activities in the diary, extracted cardiac and motion features and manual inspection of the acceleration signal. For recovery phase analysis, post-activity periods of 10 minutes were selected after each activity. For the analysis, premature beat density was calculated per classified activity, post-activity or sleep period. An example of the activity classification and beat detection for one complete test are shown in figure A1 (appendix 1).

Sample size and statistical analysis

Because of the exploratory nature of the intended objective of the complete study, a limited sample size was justified. This indicates that further data collection in the future will be warranted. To investigate the differences between the density of premature beats during- and after exercise, the exact sign test was used. A Mann-Whitney U test was performed to determine if there were statistical differences in the density of premature beats related to gender, medication intake or comorbidities. Because the sample size of patients with medication intake and comorbidities is rather low, the analysis will be performed but no conclusions will be drawn. A Spearman's rank-order correlation test was performed to investigate the relationship between the patient characteristics (age, BMI) and the density of premature beats.

RESULTS

Patient characteristics

The study population consisted of 16 individuals; 9 male, 7 female. Average age was 67.1 ± 13.7 years and average BMI was 27.7 ± 5.7 kg/m^2. In the entire study population, 93.8% uses medication and 62.5% of the patients had a medical condition. Patients' demographics are displayed in table 1.

Table 1. Patient characteristics

	n	%
Patients	16	
Gender		
Male	9	56.0
Female	7	44.0
Medication	15	93.8
Anti-coagulation	12	65.0
Statin	9	56.3
Beta blockers	8	50.0
Anti-arrhythmic drug I	4	25.0
Anti-arrhythmic drug III	3	18.8
Calcium channel blockers	2	12.5
Digoxin	1	6.3
Medical condition	10	62.5
Cardiovascular diseases	5	31.3
Other	3	18.8
Stroke	2	12.5
Hypertension	1	6.3
Diabetes	1	6.3

The VPB and SVPB density of premature beats during- and after activity, total density per daytimes, medication intake and medical conditions were tested for a normal distribution by assessing the Shapiro-Wilk's test ($p>.05$). None of these variables were normally distributed. Shapiro-Wilk's test for the density of VPBs during- and after cycling showed a significant value, however due to the small sample size (n=5) it is still considered not normally distributed. Because transformation is not possible, non-parametric tests are performed.

Premature beats during- and after activity

Table 2 shows an overview of the density of SVPBs and VPBs during and after activity. The premature beat density was calculated by first measuring the total amount of premature beats and then adjusting by the total duration of the specific activity. Of the 16 patients included in this study, 14 patients performed walking activities and 5 patients performed cycling activities. Total walking time for all patients was 7 hours and 19 minutes. The total cycling time was 4 hours and 16 minutes.

Table 2. Descriptive statistics of the SVPB and VPB densities during- and after activity

Activity	N	Minimum	Maximum	Median	Mean	sd	p-value
SVPB density during walking	14	.0	28.2	.00	2.4	7.5	.688
SVPB density after walking	14	.0	30.6	.10	2.5	8.1	
SVPB density during cycling	5	.0	29.2	.00	5.9	13.0	1.00
SVPB density after cycling	5	.0	29.2	.00	6.7	12.7	
VPB density during walking	14	.0	15.8	.35	2.6	4.7	.754
VPB density after walking	14	.0	13.8	.35	1..9	3.7	
VPB density during cycling	5	.0	5.6	.60	2.3	2.7	1.00
VPB density after cycling	5	.0	9.4	.70	3.0	4.1	

The exact sign test was used to investigate the differences between the density of premature beats during- and after activity. On average the participants showed slightly higher SVPB density after the exercise, compared to during exercise for both walking and cycling. Data are medians unless otherwise stated. Patients had a higher SVPB density after walking (.10) compared to during walking (.00); a median difference of .00 % SVPB, p=.688. Patients had a comparable SVPB density after cycling (.00) compared to during cycling (.00); a median difference of .00 % SVPB, p=1.00.

Regarding the mean density of VPBs, for walking the density was higher during walking, compared to after walking. The mean density of VPBs during cycling was lower compared to the density after cycling. Patients had a comparable VPB density after walking (.35) compared to during walking (.35); a median difference of .00 % VPB, p=.754. Patients had a higher VPB density after cycling (.70) compared to during cycling (.60); a median difference of .00 % VPB, p=1.00.

There was no statistical difference found during compared to after activity for both SVPBs and VPBs.

Premature beats per day time

Table 3 shows an overview of the total density (summed SVPBs and VPBs) in the morning, the afternoon and during sleep. Like the previous analysis, the total amount of premature beats was measured and density was calculated after adjustment for total amount of time for the specific daytime. Total time in the morning for all patients was 76 hours and 27 minutes. Total time in the afternoon was 165 hours and 24 minutes. Total time in during sleep was 124 hours and 40 minutes. All 16 patients were included in this analysis.

Table 3. Descriptive statistics of the total premature beat densities per day time

Activity	N	Minimum	Maximum	Median	Mean	sd	p-value
Total density during morning	16	.0	28.0	1.40	4.1	7.5	.774
Total density during afternoon	16	.0	25.9	1.00	3.4	6.6	.774
Total density during sleep	16	.0	27.7	0.95	4.2	7.1	

The exact sign test is also used to investigate the differences between the density of premature beats per daytime. The mean density for total premature beats was slightly higher in the morning and during sleep. Data are medians unless otherwise stated.

Patients had a higher total density in the morning (1.40) compared to in the afternoon (1.00); a median difference of .00 %, p=.774. Patients had a higher total density in the morning (1.40) compared to during sleep (.95); a median difference of .00 % SVPB, p=.549. Patients had a higher total density in the afternoon (1.00) compared to during sleep (.95); a median difference of .00 % SVPB, p=.774.

There was no statistical difference found between the different times of the day for the total density of premature beats.

Relation between premature beats and patient characteristics

A Mann-Whitney U test was performed to determine if there were differences in premature beats between male and female patients. The results are presented in table 4. Distributions of the engagement scores for male and female patients were not similar, as assessed by visual inspection. The density of VPBs during walking for male (mean rank = 9.75) and female (mean rank = 4.50) was statistically significantly different, (U = 145, z = -1.488, p = .020) (figure 1, left). The density of total premature beats during the morning for male (mean rank = 10.78) and female (mean rank = 5.57) was statistically significantly different, (U = 145, z = -1.488, p = .031) (figure 1, right).

Table 4. Statistical results of Mann-Whitney U test for differences of premature beats between male and female

	Male (mean rank)	Female (mean rank)	p-value
SVPB density during walking	8.19	6.58	.491
SVPB density during cycling	3.25	2.00	.800
VPB density during walking	9.75	4.50	.020*
VPB density during cycling	3.50	1.00	.400
Total density during morning	10.78	5.57	.031*
Total density during afternoon	6.43	10.11	.142
Total density during sleep	6.36	10.17	.114

* Significant difference between male and female (p<.050)

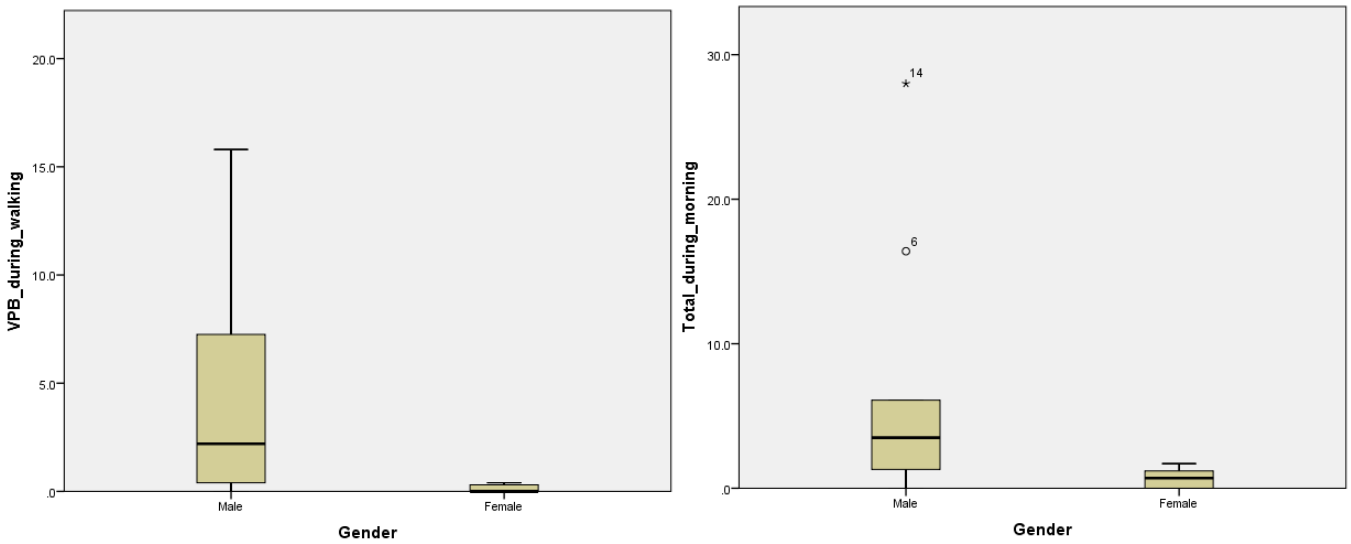

Figure 1. Boxplot of the relation between gender and the density of VPBs during walking (left) and the total density of premature beats in the morning (right).

A Spearman's rank-order correlation test was performed to investigate the relationship between the patient characteristics (age, BMI) and the density of premature beats. The results are presented in table 5. There was a positive correlation between BMI and the total amount of premature beats during sleep, $r_s(14) = .542$, p=.030 (figure 2, left). Preliminary analysis showed the relationship to be monotonic, as assessed by visual inspection of a scatterplot. There was a trend towards a positive correlation between BMI and the total density of premature beats during the morning, $r_s(14) = .483$, p=.058 (figure 2, right). Furthermore there was a trend towards a positive correlation between age and the density of SVPBs during walking, $r_s(12) = .494$, p=.073.

Table 5. Statistical results for Spearman's rank-order correlation test for relation between patient characteristics and premature beat density

	Age (r_s)	p-value	BMI (r_s)	p-value
SVPB density during walking	.494	.073†	-.059	.842
SVPB density during cycling	.671	.215	.671	.215
VPB density during walking	-.043	.884	.380	.180
VPB density during cycling	-.200	.747	.400	.505
Total density during morning	-.182	.500	.483	.058†
Total density during afternoon	.054	.843	.312	.239
Total density during sleep	-.017	.950	.542	.030*

* Significant relation (p<.050), † Trend towards significant relation (.050<p<.100)

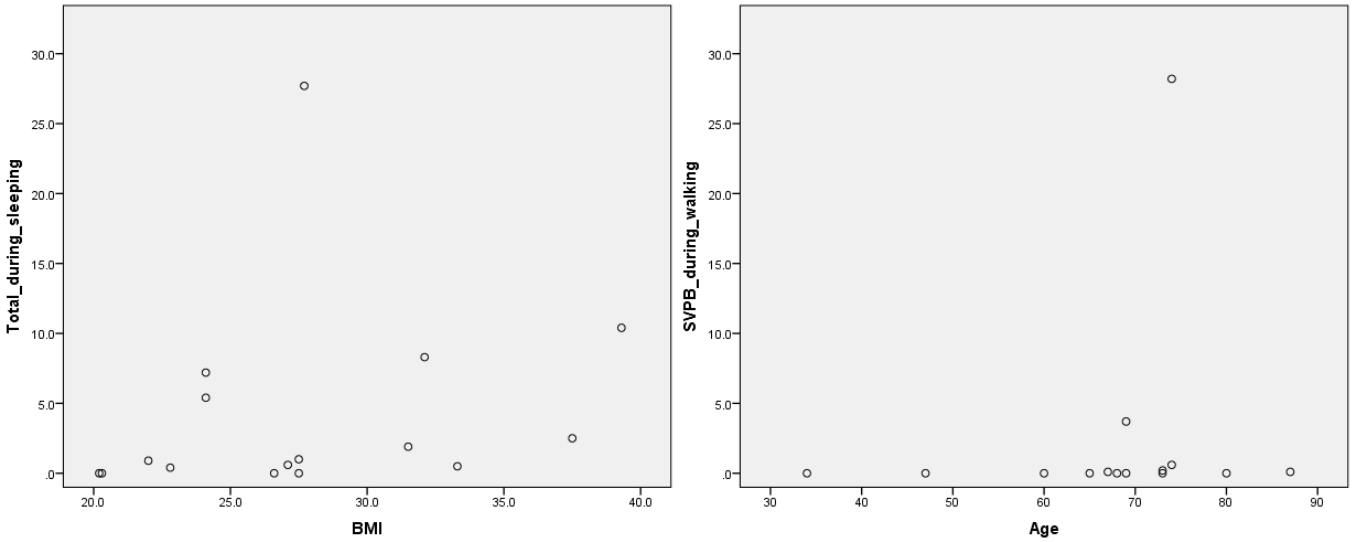

Figure 2. Scatterplot of the relation between BMI and the total density of premature beats during the night (left) and the relation between age and the density of SVPBs during walking (right)

The effect of medication

A Mann-Whitney U test was performed was performed to determine if there were differences in premature beats between patients having different kind of medication intake.

Beta blockers

Distributions of the engagement scores for beta-blockers or no beta-blockers were not similar, as assessed by visual inspection. The density of premature beats during the morning for patients using beta-blockers (mean rank = 6.12) and no beta-blockers (mean rank = 10.88) were statistically significantly different, U = 145, z = -1.488, p = .050. The density of premature beats during the afternoon for patients using beta-blockers (mean rank = 5.75) and no beta-blockers (mean rank = 11.25) were statistically significantly different, U = 145, z = -1.488, p = .021.

Anti-arrhythmic drug III

Distributions of the engagement scores for Anti-arrhythmic drug III or no Anti-arrhythmic drug III were not similar, as assessed by visual inspection. The density of VPBs during walking for patients using Anti-arrhythmic drug III (mean rank = 12.0) and no Anti-arrhythmic drug III (mean rank = 6.27) were statistically significantly different, U = 145, z = -1.488, p = .038. The total density of premature beats during the morning for patients using Anti-arrhythmic drug III (mean rank = 13.67) and no Anti-arrhythmic drug III (mean rank = 7.31) were statistically significantly different, U = 145, z = -1.488, p = .039. The total density of premature beats during the sleeping for patients using Anti-arrhythmic drug III (mean rank = 13.67) and no Anti-arrhythmic drug III (mean rank = 7.31) were statistically significantly different, U = 145, z = -1.488, p = .039.

Further, no statistically significant relation was found between the medication intake and premature beats. All p-values are presented in table 6.

Table 6. Statistical results of Mann-Whitney U test for the relation between premature beats and medication intake

	Anti-coagulation N=12 (p-value)	Statin N=9 (p-value)	Beta-blockers N=8 (p-value)	Anti-arrhythmic drug I N=4 (p-value)	Anti-arrhythmic drug III N=3 (p-value)	Calcium channel blockers N=2 (p-value)	Digoxin N=1 (p-value)
SVPB density during walking	.374	.950	.108	.635	.291	.352	.571
SVPB density during cycling	.400	.400	.400	1.00	.400	.800	n.a.
VPB density during walking	.945	.852	.142	.635	.038*	.549	.714
VPB density during cycling	1.00	.100	.400	.800	1.00	1.00	n.a.
Total density during morning	.521	.408	.050*	.862	.039*	.817	1.00
Total density during afternoon	.599	.299	.021*	.379	.082†	1.00	1.00
Total density during sleep	.862	.210	.382	.862	.039*	.817	.750

* Significant relation ($p<.050$), † Trend towards relation ($.050<p<.100$), n.a. Not available

The effect of comorbidities

No significant effect was found with the Mann-Whitney U test between comorbidities and premature beats. All p-values are presented in table 7.

Table 7. Statistical results of Mann-Whitney U test for the relation between premature beats and comorbidities

	Cardiovascular diseases N=5 (p-value)	General comorbidities N=3 (p-value)	Stroke N=2 (p-value)	Hypertension N=1 (p-value)	Diabetes N=1 (p-value)
SVPB density during walking	.733	.352	1.00	.741	n.a.
SVPB density during cycling	1.00	n.a.	n.a.	n.a.	n.a.
VPB density during walking	1.00	.549	.198	1.00	n.a.
VPB density during cycling	1.00	n.a.	n.a.	n.a.	n.a.
Total density during morning	1.00	.111	.700	.250	.625
Total density during afternoon	.377	.239	.600	.375	.750
Total density during sleep	.913	.521	.600	.250	.500

n.a. Not available

DISCUSSION

The aim of this study was to investigate the relationship between daily activities (walking and cycling) and the occurrence of premature beats in patients receiving a Holter recording for 24 or 48 hours. The reason for this study was that new insights were needed to inform patients who have complaints by having premature beats, about what daily activities induce regarding the occurrence of premature beats.

In this study population, consisting of 16 individuals, there was no significant effect found between during- and after walking or cycling and the occurrence of premature beats. The clinical significance of premature beats during exercise has been identified in several studies (17). A study of Frolkis at all. (10) showed that frequent VPBs during exercise or during the recovery phase after the exercise, predicted an increased risk of death (10). A possible reason for not finding any significant results could be that we have not looked into the increase of heart rate, or intensity for the specific activities. Moreover, the study of Frolkis at all. used clinical data from controlled clinical exercise and not during daily living. Furthermore, in the current study only post-activity periods are taken into account in this study, disregarded any baseline measurements, pre-activity periods or non-activity periods.

In addition, the relationship between the time of the day, patient characteristics, medicine intake, and comorbidities and premature beats was investigated. No effect was found between the total density of premature beats and the time of the day. Further results implicated that the density of VPBs during walking and the total density of premature beats in the morning was significantly higher in males compared to females ($p=.020$, $p=.031$). An increase in BMI was associated with an increase in total amount of premature beats during the night ($p=.30$) and there was a trend towards a significant correlation between BMI and the total density of premature beats during the morning ($p=.058$). A recent study with >25.000 subjects performed by Sabbag et al. (21) concluded that obesity is independently associated with an increased likelihood of VPBs during exercise. However, in our study we could not find the relation between a high BMI and premature beats during activity, but we did find a relation between BMI and premature beats over the day. Furthermore, there was a trend towards a positive correlation between age and the density of SVPBs during walking ($p=.073$). This result is supported by literature, which concluded that both the amount of SVPBs and VPBs significantly increase with an increased age (22-24).

In this population, a significant effect was found for the intake of beta-blockers for the total density of premature beats during the morning ($p=.050$) and the total density of premature beats during the afternoon ($p=.021$). Furthermore, there was a significant effect found of Anti-arrhythmic drug III on the density of VPBs during walking ($p=.038$), the total density of premature beats during the morning ($p=.039$) and the total density of premature beats during sleep ($p=.039$). However, these results are expected because both of these medications are used as a therapy for cardiac arrhythmias and premature beats, the amount of patients having medication was not sufficiently large to draw any conclusions. There was no significant relation

found between comorbidities and premature beats, but also here applies the small amount of patients. Previous literature indicated that hypertension and cardiovascular diseases correlates with exercise induced premature beats (11, 25).

A known limitation of this study was the small sample size of only 16 patients. No sample size calculation was done regarding the current research question before execution of this study, because of the observational nature of the study and the absence of prior data to assess premature beats variability between patients during free-living and during common daily life activities. Furthermore the results are based on 24- and 48-hour recordings, though an optimal recording for premature beats is seven days (26). Furthermore, an unexpected limitation was the low occurrence of daily activities performed by the patients during this trial. The reason for this is probably that it was not indicated in advance to the patients that we expected them to perform daily activities like walking or cycling. This should be improved in further research.

A strength of this study is that activity and post-activity classification is not only based on patient's diaries, but also on 3-axial accelerometer data and an automatic activity classification algorithm based on key feature of body movement describing the pattern of the targeted activities. This resulted in a very precise identification of the temporal onset and termination of several free-living activity tasks.

Participating in habitual physical activity may not result in a larger number of premature beats in patients with suspected cardiac arrhythmia. In this target group, presence of premature beats should not result in reducing active lifestyle. A clear cause-effect relationship between daily activity and premature beats is therefore unlikely.

CONCLUSION

No relation was found between daily activities and the occurrence of premature beats. However, important findings that correspond with previous study results are a positive relation between BMI, age and premature beats. Because the study population was small, additional research needs to be performed to confirm the results.

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Appendix 1.

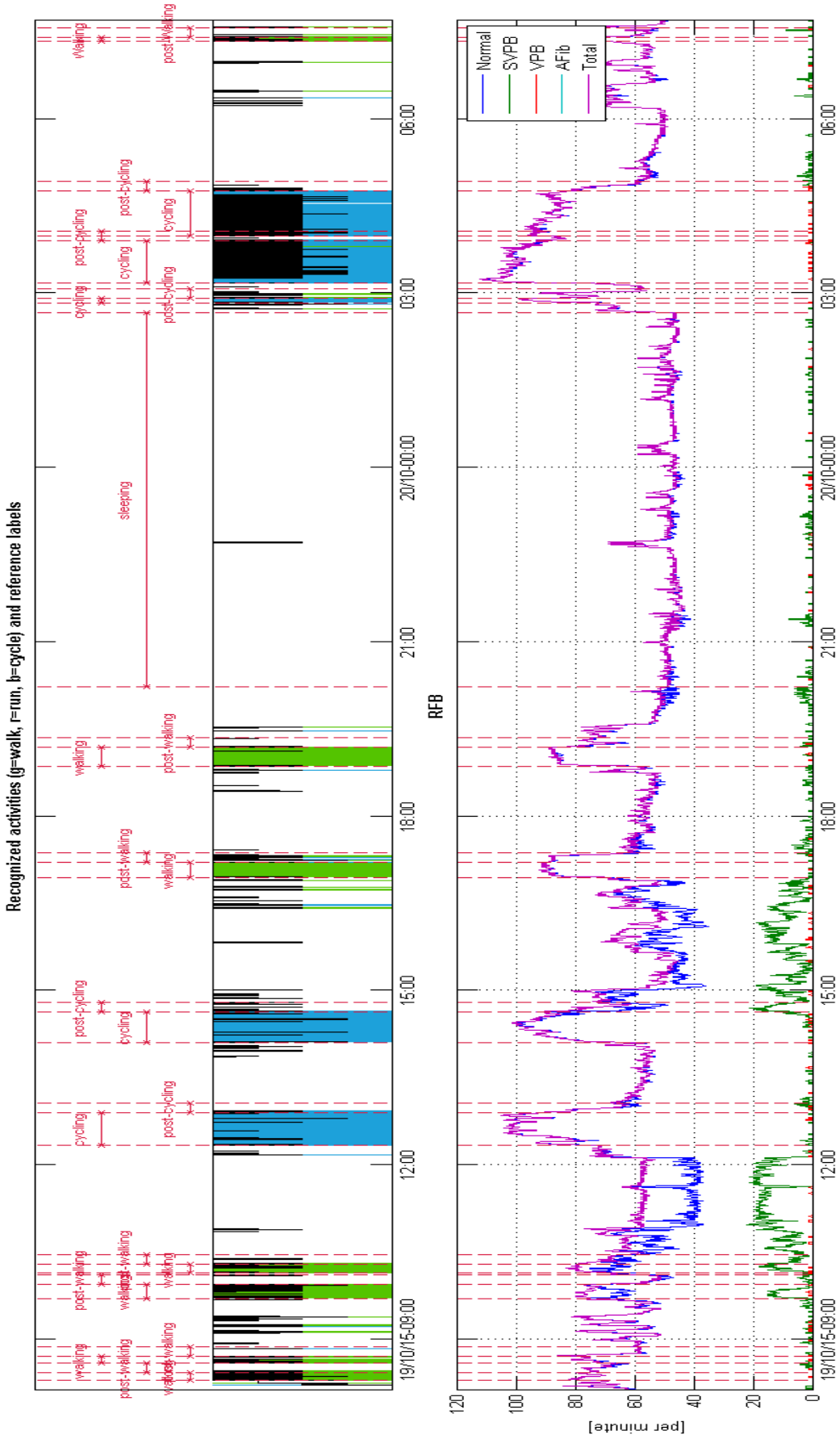

Figure A1. Example activity classification (top, bleu=cycling, green=walking) and beat detection (bottom) or one measurement