KAUNAS UNIVERSITY OF TECHNOLOGY

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METHODS FOR UNOBTRUSIVE MONITORING OF PATIENTS WITH FRAILTY SYNDROME

Doctoral dissertation
Technological Sciences, Electrical and Electronic Engineering (T 001)

Kaunas, 2023

This doctoral thesis was prepared at Kaunas University of Technology, Department of Biomedical Engineering Institute during the period of 2019–2023.

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Edited by: English language editor Dr. Armandas Rumšas (Publishing House *Technologija*), Lithuanian language editor Aurelija Gražina Rukšaitė (Publishing House *Technologija*).

The official defense of the dissertation will be held at 10 a.m. on 26 September 2023 at the public meeting of Dissertation Defense Board of Electrical and Electronic Engineering Science Field in Rectorate Hall of Kaunas University of Technology.

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Doctoral dissertation was sent out on 25 August, 2023.
The doctoral dissertation is available on the internet at http://ktu.edu and at the library of Kaunas University of Technology (K. Donelaičio 20, Kaunas, LT-44239, Lithuania).

KAUNO TECHNOLOGIJOS UNIVERSITETAS

DAIVARAS SOKAS

KASDIENĖS VEIKLOS NEVARŽANTYS SENATVINIO SILPNUMO SINDROMO PACIENTŲ STEBĖSENOS METODAI

Daktaro disertacija
Technologijos mokslai, elektros ir elektronikos inžinerija (T 001)

2023, Kaunas

Disertacija rengta 2019–2023 metais Kauno technologijos universiteto Biomedicininės inžinerijos institute.

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Elektros ir elektronikos inžinerijos mokslo krypties disertacijos gynimo taryba:
prof. dr. Arminas RAGAUSKAS (Kauno technologijos universitetas, technologijos mokslai, elektros ir elektronikos inžinerija, T 001) – **pirmininkas**;
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Disertacija bus ginama viešame Elektros ir elektronikos inžinerijos mokslo krypties disertacijos gynimo tarybos posėdyje 2023 m. rugsėjo 26 d. 10 val. Kauno technologijos universiteto Rektorato salėje.

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Disertacija išsiųsta 2023 m. rugpjūčio 25 d.
Su disertacija galima susipažinti interneto svetainėje http://ktu.edu ir Kauno technologijos universiteto bibliotekoje (K. Donelaičio g. 20, Kaunas, LT-44239, Lietuva).

Contents

List of terms and abbreviations

ACC	Accuracy
AUC	Area under curve
CI	Confidence interval
ECG	Electrocardiogram
EFS	Edmonton frail scale
F_1	F_1 score
FI	Feature importance
HR	Heart rate
HRR	Heart rate recovery
NYHA	New York Heart Association
PPG	Photoplethysmogram
PPV	Positive predictive value
RMS	Root mean square
RR interval	Time interval between two contractions of the ventricles
SampEn	Sample entropy
SDNN	Standard deviation of normal-to-normal RR intervals
SHAP	Shapley additive explanations
Se	Sensitivity
TUG	Timed up and go test
MAD	Mean amplitude deviation
RES	Heart rate reserve
6MWD	6-min walking distance

INTRODUCTION

Relevance of the research

Frailty syndrome is characterized by decline in the physiological reserve and vulnerability to internal (e.g., disease, surgery) and external (e.g., activities of daily living) stressors [1,2]. Frailty is becoming one of the most important challenges of the aging population [3]. It is manifested in 17% of community-dwelling adults over 60 years old [4]. The syndrome is associated with an increased risk of adverse outcomes, such as impaired mobility, disability, falls, and death [5]. Fortunately, evidence grows that frailty progression can be stopped and even reversed by the timely prescription of an appropriate exercise training program [6].

Older adults with frailty referred to open-heart surgery are prone to postoperative complications and often need longer recovery [7]. Considering the dramatically increasing number of older frail patients who enter cardiac rehabilitation programs, it becomes a serious issue deserving research attention [8]. In particular, this patient population suffers from a reduced muscle mass, lack of endurance, and decreased physiological functions which complicate cardiac rehabilitation and preclude the utilization of regular exercise training programs [9].

Exercise programs can benefit older adults with frailty, but the type, intensity, and duration of physical activity sessions, as well as exercise recommendations for home training, need to be carefully tailored to each individual to achieve rehabilitation goals without causing harm [10, 11]. However, in some cases, exercise training can become complicated. For example, after open-heart surgery, aerobic and strength exercises are typically recommended to protect the sternum, but frailty may limit the use of the conventional training methods. Instead, a tailored program may be needed to increase the muscle strength, weight, and mobility. Therefore, there is a need for informative and convenient tools to assess the effectiveness of exercise training programs, particularly when programs are intended for vulnerable patients, and they are continued outside the clinical setting.

Despite the availability of various indexes and questionnaires covering physical, physiological, cognitive, and social components, there is no universally accepted standardized tool for frailty assessment [12]. Additionally, clinical tools often require the involvement of healthcare specialists, which greatly limits their applicability beyond the clinical settings. As clinical tools are unsuitable for use outside of the clinical environment, there has been a growing interest in studying new markers, often obtained by using wearable devices, which could enable earlier identification of frailty [13]. Traditionally, research has been focusing on physical markers as the first component to get manifested in frail adults, with the slowness of gait being among the most informative in identifying frailty [13].

The growing body of evidence suggests that measures beyond those describing properties of physical activity may better reflect the physiological reserve [14]. Recent systematic review and meta-analysis reported that various heart rate (HR) measures reflecting autonomic function, namely, orthostatic heart response, spectral analysis of low and high frequency domains of HR, HR change after standing, and baroreflex sensitivity, were impaired in frail older adults compared to non-frail individuals [15]. Considering that HR measures can be affected by both psychological and physical stressors, they could serve as valuable markers for evaluating the impacts of medical, physical, and nutritional interventions in frail patients.

Frailty is a complex syndrome which encompasses various components, including bthe physiological reserve, physical abilities, and the cognitive function. Therefore, it is essential to accurately identify the specific frail components in an individual patient and implement personalized exercise programs to strengthen the affected individuals [16]. Unfortunately, this area of research has not yet received the necessary attention, and still there is a lack of algorithmic solutions to that problem.

Scientific-technological problem and working hypothesis

Currently, the clinical practice for assessing frailty is limited to in-clinic evaluations. However, wearable technology has advanced to the point where frailty can potentially be assessed outside of the clinical setting. However, there are several challenges which arise when attempting to assess frailty in daily living by using wearables. These challenges include detecting physical stressors and the evaluation of the status of physiological functions attributed to frailty.

Scientific-technological problem: How can information obtained from wearable-based biosignals be utilized to assess an individual's frailty status in activities of daily living?

The working hypothesis: Wearable-based monitoring is a suitable alternative to clinical tests for assessing frailty outside of the clinical setting.

Research object

The research is based on the development and investigation of signal processing algorithms for unobtrusive monitoring of the frailty status and the related physiological functions.

The aim of the research

To develop, investigate, and validate algorithms for unobtrusive monitoring of the frailty status in the activities of daily living.

The objective of the research is to develop, investigate, and validate signal processing algorithms which enable the assessment of an individual's frailty status on the grounds of wearable-based biosignals. Specifically, the thesis proposes and explores algorithms for:

1. detecting physical stressors;
2. assessing kinematic properties;
3. assessing the heart rate response to physical stressors;
4. identifying the frailest physiological functions.

Scientific novelty

With an increasing number of patients with frailty being referred for surgery, there is a need for convenient tools which would help to improve the understanding of the effectiveness of exercise-based rehabilitation [9]. Accordingly, this doctoral thesis proposes and investigates a wearable-based approach for unobtrusive assessment of frailty. The majority of previous research has focused on identifying frailty or pre-frailty in older adults. However, the feasibility of capturing subtle changes in the frailty status during exercise training has not yet been deeply explored. This thesis fills this research gap by examining the suitability of kinematic and HR response measures for tracking the frailty trajectory during exercise-based rehabilitation, by specifically focusing on walking and stair-climbing as representative activities. The approach has been comprehensively explored on patients after supervised inpatient rehabilitation with an increased intensity, as well as unsupervised home-based exercise training with a reduced intensity. The potential applications of this approach include assessing the frailty status during home-based exercise training and remote monitoring of frail patients for early the detection of frailty impairment.

The main finding of the analysis of algorithms for assessing the kinematic properties by using wearable-based biosignals is that most kinematic measures improved in the majority of patients who also exhibited an improvement in their frailty status after inpatient rehabilitation. No notable change in kinematic measures was observed after completing the home-based exercise training program, which corresponds well with only a minor deterioration in the frailty status as indicated by a clinical reference.

The main finding of the analysis of algorithms for assessing the heart's response to physical stressors is that the HR response improved in most patients after a surgery. The improvement was the most obvious in the intervention group to whom home-based exercise training was assigned. This suggests home-based training as a proper intervention to improve the physiological reserve. When considering the applicability of submaximal tests, walking and stair-climbing were found to be the most suitable to induce the HR response sufficient enough to follow the trends of measures observed when using veloergometry.

Finally, an interpretable machine learning-based algorithm for identifying clinically informative features that provide information on the frailest components of an individual patient has been proposed. The use of interpretable machine training allows to associate the frailty status with specific frailty-describing features, which, in turn, can provide additional information to healthcare specialists for the development of personalized training programs. Consequently, the proposed approach has the potential to enhance the comprehension of frailty in individual patients and facilitate the prescription of tailored interventions for more effective rehabilitation.

Practical significance

1. The proposed approach for assessing and interpreting the frailty status can be valuable in the following applications:
   (a) Assessment of the frailty status in the course of home-based exercise training.
   (b) Remote monitoring of frail patients aiming at an early detection of frailty impairment.
   (c) Aid for clinicians in designing tailored exercise training programs.
   (d) Aid for clinicians in understanding the frailest components of an individual patient.
2. The approach and algorithms provided in this thesis were developed in the framework of the projects *Unobtrusive technologies for monitoring of autonomic nervous system function in patients with frailty syndrome - FrailHeart* funded by the Research Council of Lithuania (S-MIP-20-54, 2020–2022) and *Interpretable Machine Learning for Assessing Frailty Syndrome - intFrail* funded by the Research and Innovation Fund of Kaunas University of Technology (Project Grant No. PP2022/58/2, 2022).

Approval of the research

This doctoral thesis relies on two main articles published in the international scientific journals with the impact factor referred in the *Clarivate Analytics Web of Science* database. A further group of two articles, published in the international scientific journals with the impact factor, is closely related to the research topic. The essential results have been presented in *BIOSIGNALS 2021: 14th International Conference on Bio-inspired Systems and Signal Processing* and *19th Nordic-Baltic Conference on Biomedical Engineering and Medical Physics*. The paper presented at the *BIOSIGNALS 2021* conference was awarded the title of the best student paper.

The statements presented for defense

1. Stair-climbing and walking can be submaximal alternatives to conventional clinical exercise tests, and the type of physical activity can be determined in free-

living conditions by analyzing acceleration signals acquired when using wearables.

2. Tracking the frailty trajectories during exercise training after an open-heart surgery by relying on kinematic measures obtained from a single wearable sensor can be an alternative to the conventional clinical exercise tests.
3. HR response to physical stressors can be considered for assessing the effectiveness of exercise training programs in patients with frailty.
4. The identification of the frailest components by using an interpretable machine learning-based approach is a feasible strategy.

Structure of doctoral thesis

The doctoral thesis is organized as follows. Section 1 is designated to the analysis of the relevant scientific literature with respect to the clinical significance of frailty and the currently used approaches for frailty assessment. Section 2 presents the database used for the development, investigation, and validation of the algorithms. Sections 3 and 4 describe the algorithms and the results for the identification of physical stressors, the assessment of kinematic properties, the assessment of HR response, and the identification of the frailest components.

Parts of the thesis have been quoted verbatim from the previously published articles: [17, 18].

The thesis consists of 112 pages, 20 figures, 14 tables. It features 168 references.

Work done in collaboration

Research on the characterization of kinematic properties was performed in collaboration with Dr. Monika Butkuvienė (Biomedical Engineering Institute, KTU), whereas research on the characterization of the HR response was performed in collaboration with Assoc. Prof. Raquel Bailón-Luesma (Biomedical Signals Interpretation and Computational Simulation group, University of Zaragoza, Spain). Database of wearable-based biosignals and reference clinical data was recorded by healthcare specialists (Eglė Tamulevičiūtė-Prascienė, Aurelija Beigienė, Vitalija Barasaitė) under the supervision of Prof. Raimondas Kubilius representing Kulautuva Rehabilitation Hospital of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics.

1. OVERVIEW

This chapter introduces the clinical relevance of assessing frailty. It emphasizes the potential role of cardiac autonomic imbalance on the acceleration of frailty progression. Furthermore, the chapter overviews various approaches towards wearable-based assessment of frailty, specifically focusing on gait, balance, and heart rate measures. Emphasis is placed on the need to develop unobtrusive means for routine frailty assessment outside of the clinical settings.

1.1. Clinical Relevance and Remaining Challenges

Frailty is a condition commonly observed in older adults and is characterized by a decline in the physiological reserve and an increased susceptibility to physical stressors [19]. This decline occurs across multiple organ systems, and results in various adverse healthcare outcomes, including mobility loss, disability, emergency visits, institutionalization, hospitalization, and death [1]. Although frailty is often chronic and progressive, it is not always a one-way progression towards complete decline. Proper interventions, such as exercise training, have shown potential to improve or even reverse frailty, thus indicating that frailty may be amenable to intervention strategies aimed at mitigating adverse effects [6, 20, 21].

Clinical observations indicate that the relationships between the manifestations of frailty may be structured into a cycle of naturally occurring events that perpetuate themselves [22]. The theory proposes that the cycle of frailty starts with the manifestation of some trigger which initiates a cascade of events leading to an aggregated syndrome. It was also presumed that different initial manifestations may lead to varying rates of progression towards frailty [23]. The concept of the cycle of frailty was first postulated by Fried as illustrated in Fig. 1.1. The various physiological functions taking part in the cycle form the basis for the frailty assessment tool currently known as *Fried's phenotype*.

The growing evidence suggests that cardiac autonomic imbalance may be an accelerating factor of the frailty progression. Despite the multitude of studies, the physiological relationship of cardiac autonomic control and frailty still remains unclear, mostly because both cardiac autonomic dysfunction and cardiovascular disease may be contributors to frailty. This reasoning can be supported by studies demonstrating a higher prevalence of cardiac autonomic dysfunction in both frail and pre-frail older adults [24]. A reduced cardiac autonomic control may lead to lower physical activity, reduce the ability to maintain homeostasis, and thus increase the vulnerability to stressors [14, 25, 26].

The increasing number of frail patients entering cardiac rehabilitation programs is a major concern as frail adults are at a higher risk for surgical interventions, prolonged recovery, postoperative complications, and in-hospital mortality [8]. Frailty

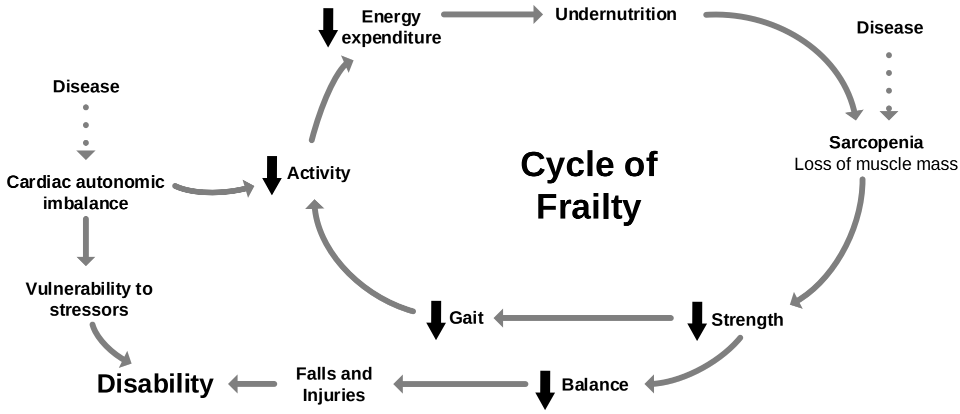


Figure 1.1. Cycle of frailty involving cardiac autonomic imbalance.

in patients who have undergone an open-heart surgery, where sternum protection is mandatory, can impact the type and intensity of exercise training programs, often limiting the use of regular programs [9]. Furthermore, individual responses to tailored exercise training can vary, and therefore necessitate convenient and informative tools to routinely assess the effectiveness of a training program, especially when training continues at home.

Exercise programs that include resistance, aerobic, balance, and coordination exercises have shown promise in improving the gait, balance, and physical performance in adults with frailty, although the optimal characteristics of these exercises (such as the type, frequency, and duration) remain unclear according to previous studies [3, 10, 27, 28]. Determining the optimal exercise characteristics is challenging due to the variability in program preparation across different rehabilitation clinics, which complicates the comparison of various programs.

To tackle these challenges, it is crucial to focus research efforts on developing comprehensive and practical approaches for frailty assessment that can be applicable outside of the clinical setting.

1.2. Clinical Assessment of Frailty

Various tools and approaches are used in clinics to assess frailty, typically involving the evaluation of multiple aspects of an individual's physical, psychological, cognitive, and social functioning (see Table 1.1). Fried's frailty phenotype is commonly used as a clinical indicator of the frailty status, particularly in studies involving physical activity-describing measures [13], since it solely focuses on such physical components as weight loss, weakness, slow gait speed, exhaustion, and low physical activity [22]. Other tools, such as the Edmonton Frail Scale (EFS), also account to social, cognitive, and nutritional aspects [29]. Despite being a subjective approach, the EFS has shown high reliability and validity in various studies [12, 29, 30].

Table 1.1. Summary of the most commonly applied indexes to assess frailty status.

Index	Components evaluated	Assessment type	Need of special equipment	Studies
Fried frailty phenotype	Physical	Objective	Needed	[31]
Tilburg frailty indicator	Physical, cognitive, social	Mixed	Needed	[32]
Groningen frailty indicator	Physical, cognitive, social	Subjective	Not needed	[33]
Edmonton frail scale	Physical, cognitive, social, clinical	Mixed	Not needed	[29]
PASE	Physical	Objective	Needed	[34]
FES-I	Physical, clinical	Subjective	Not needed	[35,36]

PASE – physical activity scale for the elderly; FES-I – falls efficacy scale-international.

1.3. Wearable-based Assessment of Frailty

1.3.1. Stressors in patients with frailty

Stressors in patients with the frailty syndrome refer to internal or external factors or conditions which can put additional strain on their already compromised functioning. These stressors can worsen the frailty status and increase the risk of adverse health outcomes.

The primary internal stressors experienced by patients with the frailty syndrome are illnesses, infections, surgeries, and medical procedures [37]. Due to their weakened immune systems, these patients are more susceptible to infections or illnesses, which can further deteriorate their physical condition and increase the risk of complications. Additionally, surgical procedures or other medical interventions can impose a significant physical stress, as their frailty may render them more vulnerable to the physiological and metabolic demands of the procedure, as well as the postoperative recovery [38].

Out of external stressors, walking and stair-climbing can be considered as common physical stressors due to the challenges they pose to their compromised physical functioning. Frailty can impact an individual's ability to walk or climb stairs safely and efficiently. Based on the percentages reported in [39], 18% of older adults with frailty could not walk one bus-stop distance (about 50 m) and climb a flight of stairs. Other physical stressors, such as those experienced in the environment (e.g., extreme temperatures or inadequate housing conditions) can also impact the physical health of patients with the frailty syndrome, as they may have reduced ability to adapt or cope with such stressors [2].

1.3.2. Assessment of gait and balance

Gait and balance are fundamental aspects of the motor function which play a critical role in mobility and the overall functional ability in older adults. Gait refers to the pattern of movement while walking, including the rhythm, speed, and coordination of steps whereas balance refers to the ability to maintain a stable posture under stationary or dynamic conditions. Gait and balance can be influenced by various factors, including age-related physiological changes, musculoskeletal disorders, sensory deficits, and cognitive decline [40]. These factors contribute to changes in the gait patterns, such as a decreased step length, a reduced walking speed, altered foot placement, and increased stride variability. Additionally, older adults may exhibit impaired balance control, manifested by decreased postural stability, increased postural sway, and reduced ability to recover from perturbations [41].

Numerous assessment tools are available for evaluating the gait and balance. These may include clinical assessments, such as fixed distance walk, timed up-and-go tests, and balance tests, as well as advanced technologies, such as wearable sensors and motion analysis systems [42]. Obviously, utilizing specialized equipment for routine assessments of frailty is not practical. Therefore, there are ongoing efforts to gain a deeper understanding of how frailty is manifested and to develop novel approaches which can be applied in non-clinical settings.

A longitudinal study on frailty development revealed exhaustion, weakness, low physical activity, and a slow gait among the initial signs to appear [21]. Consequently, it is unsurprising that impairment in the physical function, as reflected in the measures of physical activity, gait, and balance, has been found to be valuable in distinguishing between different frailty statuses [13, 43].

The prevalent approach for estimating the physical activity, gait, and balance measures involves the use of wearable inertial sensors to capture kinematic signals [12]. Among these measures, the gait speed has been identified as the most powerful indicator for identifying frailty, while other physical activity measures show moderate correlation with the frailty status [13,43,44,45]. Balance measures, on the other hand, tend to be less powerful than physical activity and gait measures in discriminating frailty statuses [13,43]. The most common kinematic measures are given in Table 1.2.

Typically, wearable-based kinematic measures are estimated during various clinical tests which usually require supervision [39]. However, considering monitoring

Table 1.2. Summary of kinematic measures.

Measure	Wearable-based implementation	Kinematic property	Main findings related to the measure	Studies
Gait speed	Simple	Gait	One of the most sensitive measures for identification of pre-frailty	[13, 42, 43, 43, 46, 47, 48, 49, 50]
Cadence	Simple	Gait	Motor function assessment measure characterizing mobility of lower extremities	[42, 43, 47, 48, 49, 51]
Mean amplitude deviation	Simple	Gait	Measures physical activity levels, disregarding the physical activity type	[44, 52]
$6MWD$	Simple	Gait	Can be used to assess functional performance in free-living	[53]
Number of steps	Simple	Gait	Used to evaluate endurance, can be assessed for different time intervals	[43, 53]
Gait irregularity	Simple	Gait	Describe the predictability of walking cycles	[51, 54]
Stride length	Complex	Gait	Reported significant reduction for patients with cognitive frailty	[42, 43, 47, 49, 50]
Swing phase %	Complex	Gait	Reported reduction of measure in elderly patients	[48, 49, 50, 54]
Stance phase %	Complex	Gait	Reported increase of measure in elderly patients	[48, 49, 50, 54]
Timed up-and-go test	Complex	Gait	Used to assess functional performance in patients with frailty	[29]
Sway range	Simple	Balance	Reported increase of measure in patients with frailty	[13, 43, 54, 55]
Sway area	Simple	Balance	Reported increase of measure in patients with frailty	[13, 43, 55]
Sway irregularity	Simple	Balance	Reported increase of measure in patients with frailty	[50, 55]
Lissajous index	Simple	Balance	Evaluates the symmetry of movement during physical activity	[56]
Step width	Complex	Balance	Associated with frailty	[47, 57]
Double support %	Complex	Balance	Association between frail and not frail, and prefrail and not frail	[47, 49]
CoP length variability	Complex	Balance	Can be assessed during physical activity or during quite standing	[43]
Asymmetry	Complex	Balance	Considerable cognitive effort is needed to maintain gait symmetry	[50, 51, 54]

outside the clinical environment, it may be more relevant to focus on common daily life activities, such as walking or stair-climbing, which are integral to most individuals' daily routines, except for severely frail adults [39].

1.3.3. Assessment of the autonomic nervous system

The autonomic nervous system (ANS) functions through a series of complex neural pathways involving nerve cells, or neurons, which transmit signals to various target tissues and organs throughout the body. The ANS plays a critical role in regulating many vital physiological processes in the body, and in ensuring the proper functioning and adaptation to the changing conditions, and its complex and coordinated activities are essential for maintaining the overall health and well-being [58].

The ANS is divided into two main branches: the sympathetic nervous system and the parasympathetic nervous system. The sympathetic nervous system is activated during stress, excitement, or danger and it is responsible for the 'fight-or-flight' responses in preparing the body for emergencies by increasing HR and diverting blood flow to muscles. On the other hand, the parasympathetic nervous system is responsible for the 'rest-and-digest' responses, thus promoting relaxation, digestion, and other essential bodily functions during the periods of rest and recovery [58].

Since the cardiovascular function is regulated by the ANS, cardiac autonomic imbalance may contribute to frailty worsening [14, 26, 59, 60], which, in turn, may decrease the capacity to maintain homeostasis when exposed to physical stressors [14, 61]. The ANS controls the rate at which the sinoatrial node produces electrical impulses; thus, abnormal HR characteristics, such as increased resting HR, decreased the HR complexity and variability, a slower and weaker HR response to physical activity, and attenuated HR recovery after exercise, often relate to the autonomic imbalance [14, 62].

The HR response to walking was investigated and linked to the frailty status [63]. The findings revealed that frail older adults exhibited a slower and weaker HR response to walking compared to non-frail individuals, which indicates the potential of HR-based markers for improving the frailty assessment. However, the study only focused on normal and rapid walking, and thus the impact of other physical stressors on the HR response remains to be explored. Furthermore, the available data only covered a short time frame of 5 seconds before and 10 seconds after the walking activity, which may limit the reliable characterization of the baseline HR. Therefore, the authors of [63] expressed a keen interest in investigating the baseline HR complexity and full HR recovery measures in future studies.

Post-exercise HR recovery is noteworthy for its established clinical value when assessing the ANS [64] and predicting the risk of cardiovascular diseases and death [65]. For this reason, it has been suggested that incorporating the HR recovery assessment into the routine clinical practice could be a cost-effective and efficient alternative to spiroergometry [66]. Normally, HR recovers exponentially with a fast decrease during the first minute after physical activity, followed by a slow gradual decay until reaching the baseline HR (see Fig. 1.2). Often, HR recovery measures characterizing the fast and slow recovery phases are investigated. The fast HR decrease occurs immediately after the end of a physical activity and is due to an increase in the parasympathetic activity driven by the deactivation of the central cardiovascular control mechanism in the brain and the abolished feedback from muscle mechanoreceptors. Meanwhile, the subsequent slow HR decrease is due to coordinated parasympathetic-sympathetic interaction mediated by the reduced feedback from muscle metaboreceptors and the adjustments in thermoregulation [67].

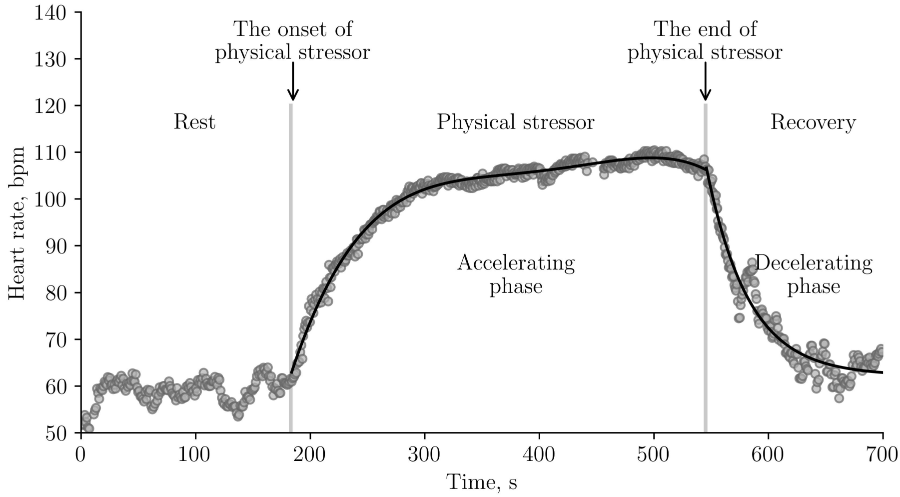


Figure 1.2. Example of a typical HR response with clearly expressed accelerating and decelerating phases.

Differently from the HR recovery which has been extensively studied, the accelerating phase of the HR response has received much less attention despite both of them reflecting the balance of the ANS [68]. An increased time-to-peak HR during walking was observed in frail older adults compared to non-frail ones [63].

The HR reserve was calculated by finding the difference between an individual's maximum heart rate and their resting HR. The HR reserve is often used to assess the chronotropic incompetence in patients with heart failure, and it indicates an impaired chronotropic response when it is below 80% when estimated at peak exercise [69].

The baseline HR measures, namely, resting HR, variability, and complexity may have a prognostic value when assessing the autonomic function in frail patients [14]. Nevertheless, baseline measures were found to be less powerful when differentiating between frail and non-frail older adults compared to the difference between the maximal and resting HR [14].

HR measures commonly used to characterize the ANS are described in Table 1.3.

Table 1.3. Summary of HR variability, HR response, and baseline HR measures.

Measure	Wearable-based implementation	Main findings related to the measure	Studies
HRR_{30}	Simple	Independent predictor of both cardiovascular and all cause mortality	[14, 64]
HRR_{60}	Simple	Reflect parasympathetic reactivation	[64, 65, 70, 71]
HRR_{120}	Simple	Even after submaximal exercise predicted all-cause mortality	[65, 71, 72]
HRR_{300}	Simple	Demonstrated increased cardiovascular and over-all mortality rates in subjects with diabetes	[64]
HR_{max}	Simple	Are associated with higher mortality	[62, 69, 73]
RES	Simple	Are associated with markedly reduced quality of life and diminished exercise capacity	[69, 74]
T_{30}	Complex	Marker of parasympathetic reactivation immediately after exercise	[64, 73]
T_{30min}	Complex	Similar measure to T_{30}, but with improved reproducibility	[64, 70]
T_a	Complex	Are reported to be different in non-frail and pre-frail/frail groups	[63, 68]
τ	Complex	Reflect both parasympathetic reactivation and sympathetic withdrawal	[64, 70, 75]
LF	Complex	Frail group presented increased power of the LF band as compared to non-frail and pre-frail groups	[59, 60, 64]
HF	Complex	Provides an index of cardiac vagal modulation	[59, 60, 64]
LF/HF	Complex	Reported reduction in individuals with a higher likelihood of frailty	[14, 60]
SDNN	Complex	Are associated with frailty	[14, 59, 63]
RMSSD	Complex	Represent the parasympathetic reactivation after the exercise	[14, 59, 60, 63, 64]
pNN50	Complex	Were reported to be different in non-frail and pre-frail/frail groups	[14, 59, 63]
SampEn	Complex	Are reduced in frail compared to non-frail adults	[14, 60]

1.3.4. Models for assessing frailty status

To better understand frailty and to facilitate its assessment, there have been attempts to assess the frailty status by using mathematical models [76, 77]. Some studies focused on the assessment of the frailty status from the epidemiological data and patient history, while others employed wearable-based data. Most wearable data-based models for frailty assessment predominantly rely on measures characterizing the physical activity, with only a handful of studies considering cardiovascular measures. A logistic regression model was used to identify frailty by assessing the physical activity features using a pendant sensor [78], whereas a convolutional neural network was implemented to identify frailty by analyzing the gait features extracted from the data of the wearable device [79]. A similar study employed a wearable sensor to predict frail and pre-frail in older adults; however, the model was trained and tested on the same participants [80]. The studies on the assessment of HR include a deep learning-based approach using a long short-term memory model for frailty identification [81], whereas, a k-nearest neighbors algorithm used different biosignals including HR to assess and predict the dependence while executing the activity of daily living [82].

1.3.5. Frailty in the presence of comorbidities

Frailty is linked to an increased prevalence of various comorbidities spanning across cardiovascular, respiratory and musculoskeletal diseases. Comorbidity refers to the coexistence of multiple medical conditions or diseases in an individual simultaneously [83, 84]. The presence of different comorbidities in frail individuals can impact the treatment effectiveness, and thus necessitate multidisciplinary or tailored approaches [85]. Moreover, the presence of multiple comorbidities in frail older adults poses a significant challenge of polypharmacy [86]. Adverse effects on the clinical course and outcomes are observed in frail patients with comorbidities, as they are more prone to hospitalization, rehospitalization, disability, institutionalization, and mortality [84, 87]. Regular evaluation of the status of these diseases can aid in managing frailty.

Cardiovascular diseases such as heart failure, coronary artery disease, peripheral vascular disease, and hypertension are common in frailty. Patients with any cardiovascular diseases, especially those with heart failure and peripheral artery disease, were more likely to become frail than those without any of those issues [88]. And, vice versa, patients with frailty face an increased risk of developing heart failure [89, 90], coronary artery disease [91, 92, 93], and peripheral artery disease [94]. Additionally, hypertension was found to be very common in frail individuals by reaching 72% [95].

While the evaluation of these conditions is predominantly carried out by using clinical tools, there is a growing interest in exploring wearable-based approaches. Attempts have been made to assess the severity of heart failure by tracking the cardiopulmonary status by wearing wearable-based bioimpedance sensors [96, 97], such as balistocardiogram and seismocardiogram [98], or detecting cardiac arrhythmias [99, 100, 101]. Additionally, wearable-based electrocardiography techniques have been proposed for detecting coronary artery disease [102, 103]. The status of peripheral artery disease has been assessed by tracking peripheral artery motion and vascular resistance by using photoplethysmography (PPG) and piezo-electric sensors [104].

Despite the numerous wearable-based alternatives to assess the blood pressure, many of them are inconvenient and obtrusive [105]. Several approaches have been investigated, including the use of wrist-based devices utilizing the oscillometric principle [106, 107], the analysis of the PPG waveform [108], and the monitoring of the radial pulse for assessing arterial stiffness [109]. However, the performance of these techniques has not been properly validated [105].

Respiratory diseases such as chronic obstructive pulmonary disease, sleep apnea, idiopathic pulmonary fibrosis and asthma are commonly occurring diseases in frail older adults. Exacerbations of chronic obstructive pulmonary disease were 42% higher in those with frailty compared to those without it [110]. This relationship may be because chronic obstructive pulmonary disease and frailty share the same risk factors, including aging, smoking, and inflammation, as well as clinical manifestations, such as fatigue, anorexia, muscle weakness, and a slowed walking speed [111].

The process of aging has a significant impact on the immune response, as it leads to a persistent pro-inflammatory state and an increased susceptibility to respiratory infections affecting the airways [112]. Furthermore, older patients may have a diminished perception of respiratory disease symptoms, such as asthma, and these symptoms are often only partially reversible [113]. Sleep problems, including sleep apnea, are reported by approximately a half of older adults, and they are exacerbated by fatigue and depression, particularly in older adults with frailty [114].

Wearable-based assessment of chronic obstructive pulmonary disease is a prominent research area, with most of the proposed assessment techniques focusing on unobtrusive respiration monitoring. Thoracic electrical bioimpedance can be used to assess a variety of respiration measures and breathing patterns [115,116]. A wearable-based digital stethoscope for monitoring auscultations and the breathing intensity can help to assess respiratory functions [117]. Additionally, high fluctuations of blood oxygen saturation can be used for detecting sleep apnea and assessing the severity of chronic obstructive pulmonary disease [118].

Musculoskeletal disorders such as sarcopenia and osteoporosis play a large role in the development of frailty. These disorders are often a result of malnutrition in frail individuals [119]. Sarcopenia, defined as an age-related progressive loss of muscle mass and strength, is often the leading condition which marks the onset of frailty [120]. Osteoporosis, which is also usually aftermath of malnutrition, is a systemic skeletal disease with the characteristics of a low bone mass and the deterioration of bone tissues. The relationship between frailty and osteoporosis relies on the fact that the worse the frailty status is, the greater is the likelihood that the individual will have osteoporosis complications and the higher is the risk of an injury [121]. Both sarcopenia and osteoporosis complicate the management of frailty by making usual exercise training less effective and even hurtful. The combination of both of these disorders makes older frail individuals even more likely to sustain injuries which often lead to disabilities [122]. Assessment of sarcopenia is largely based on the presence of a low muscle mass and a low muscle function which can be defined by low muscle strength or a low physical performance, which are similar aspects to those defining frailty [123].

1.3.6. Challenges related to the implementation of wearable-based monitoring in home environment

HR is typically obtained from an electrocardiogram (ECG) acquired through electrodes, which may be less motivating for older frail adults to use for extended periods of time. While a chest strap usually *does* cause discomfort for short-term use, wrist-worn bio-optical devices may be considered for monitoring in activities of daily living, albeit with reduced accuracy in estimation. Previous studies have shown substantial errors in estimating HR variability measures in elderly vascular patients when using reflective wrist PPG devices [124]. In our previous study involving healthy participants, we reported estimation errors of $\leqslant$19.2% for T_{30} and $\leqslant$20.7% for HR decay after 1 minute [70]. Therefore, further research is needed to determine the feasibility of estimating the HR response by using bio-optical sensors.

Various barriers, such as poor health or fear of injury and pain, often prevent older adults from exercising [125]. Therefore, it is crucial to identify individual barriers and motivators to enhance their willingness to comply with a training program. Special consideration should be given to addressing the patient's fears and providing clear explanations of the health benefits of exercise. Additionally, equipping patients with wearable devices, such as smartwatches, to record their physical activity could serve as a potential motivator [126].

The placement site of a single sensor near the body mass center, i.e., the lumbar spine or chest, is the most thoroughly investigated solution [13], probably due to the possibility to estimate balance measures. While using a chest strap for short periods does not cause notable discomfort, more convenient locations should be preferred considering the application in daily living. Despite recent advances in the sensor technology providing an opportunity to integrate inertial sensors into shoes and clothes [127, 128], these technologies are still pending for wide-scale availability. Out of wearables utilized to evaluate frailty [13], devices placed on the ankle or wrist can be a primary choice in terms of wearing comfort. However, wrist-worn devices are sensitive to arm and/or hand movements, which may affect kinematic measures. Nevertheless, the wrist-worn sensor showed considerably better classification accuracy when discriminating between robust and frail adults than the sensor placed on the lower back, which suggests that arm movements are an essential feature [129].

1.4. Conclusions of the Chapter

1. Recent advancements in wearable technologies have enabled the detection of different types of physical activity in daily living. However, these approaches have not been extensively tested on elderly and frail individuals who often face challenges in mobility. Frail individuals may exhibit uneven and asymmetrical walking patterns which can potentially impact the accuracy of algorithms for the identification of the physical activity type.
2. The initial components of frailty progression include the slowness of gait, low physical activity, exhaustion, and weakness, which can be monitored by using wearable inertial sensors. However, it is crucial to assess the feasibility of adapting the wearable-based approach for frail patients to ensure applicability in clinical practice.
3. There is a growing body of evidence indicating an association between frailty and cardiac autonomic dysfunction, which may impair the capacity to maintain homeostasis when exposed to physical stressors. Assessment of the heart rate response to physical stressors offers a convenient and non-invasive approach for evaluating cardiac autonomic dysfunction in frail adults. However, further research is needed to address the influence of errors in the heart rate acquired by using wearables so that to ensure accurate and reliable assessment in this population.

2. DATABASE

This chapter presents a study protocol and a comprehensive database comprising biosignals and reference clinical data, which is essential when examining the utility of wearable-based biosignals in assessing frailty. To explore various measures, data was gathered from patients with frailty who had undergone a cardiac rehabilitation program after open-heart surgery. The data collection took place during standardized exercise tests at three time points: upon admission to inpatient rehabilitation, upon completion of inpatient rehabilitation, and after engaging in home-based training.

2.1. Study Population

The patients after open-heart surgery who arrived at Kulautuva Rehabilitation Hospital of Kaunas Clinics (Kulautuva, Lithuania) from 19 November 2020 till 3 January 2022 were invited to participate in the study. Out of 337 patients assessed for eligibility on the first day of admittance to the rehabilitation hospital, 100 (38 females) fulfilled the inclusion criteria described in Table 2.1.

Table 2.1. Patient inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Age $\geqslant$65 years	Implanted cardiac devices
EFS score $\geqslant$4 at admittance to the rehabilitation hospital	Exercise limiting deficits
	Severe chronic heart failure (New York Heart Association Class IV)
6-min walk distance $\geqslant$150 m	Hemoglobin <9 g/dL
Agreement to participate	Wound healing disturbance
	Cognitive or/and linguistic deficits

EFS indicates the degree of fragility based on the Edmonton frail scale.

Upon arrival at the rehabilitation hospital after open-heart surgery (17.1 $\pm$ 7.4 days post-surgery), the patients were randomly assigned to the intervention and control groups. The groups were generally well-matched except for the fact there were considerably more men in the control group (Table 2.2). Both intervention and control groups participated in exercise training during inpatient rehabilitation. However, only the intervention group had to perform exercises at home for 12 weeks after the end of inpatient rehabilitation according to the individualized exercise training plan (see Sec. 2.4). The control group was asked to maintain their usual physical activity regimen.

Table 2.2. Demographic and clinical characteristics in the intervention and control groups before inpatient rehabilitation.

	Intervention	Control
Female	25	13
Male	25	37
Age, years	73.2 ± 4.8	73.4 ± 5.3
Height, cm	165.9 ± 8.6	169.4 ± 8.6
Weight, kg	74.9 ± 12.8	78.7 ± 13.2
Body mass index, kg/m^2	27.3 ± 4.8	27.4 ± 3.9
Post-surgery, days	16.6 ± 7.3	17.6 ± 7.5
Surgery		
Coronary artery bypass graft	23	33
Isolated valve	11	5
Combined	16	12
Medications		
Angiotensin-converting enzyme	37	40
Beta adrenoblockers	49	50
Calcium channel blockers	2	1
Heart failure class		
NYHA I	2	3
NYHA II	40	34
NYHA III	8	13
Comorbidities		
Atrial fibrillation	15	17
Chronic obstructive pulmonary disease	0	3
Depression	1	2
Musculoskeletal system diseases	1	3
Oncological diseases	4	8
Functional capacity		
Veloergometry duration, s	161.8 ± 97.8	154.4 ± 95.2
Peak workload, W	49.5 ± 15.8	51.0 ± 15.5
6-min walk distance, m	289 ± 86.1	291 ± 79.6
Timed up and go duration, s	8.9 ± 2.4	8.5 ± 1.7
Edmonton frail scale score	6.2 ± 1.6	6.0 ± 1.6

Certain parameter values are given as mean ± standard deviation.
NYHA indicates the heart failure class according to New York Heart Association classification criteria.

2.2. Clinical Assessment of Frailty

The degree of fragility was assessed based on the EFS [29], which involves nine domains of frailty, namely, cognition, general health status, functional independence, social support, medication usage, nutrition, mood, continence and functional performance. The EFS score was assessed by healthcare specialists at three time points: at the beginning of inpatient rehabilitation, after inpatient rehabilitation with a mean duration of 16.2 ± 2.9 days, and after home-based exercise training with a mean duration of 104.2 ± 23.0 days. At the beginning of inpatient rehabilitation, the EFS score ranged from 4 to 9 and from 4 to 10 in the intervention and control groups, respectively.

2.3. Data Acquisition

Electrocardiogram and triaxial acceleration signals, sampled at 130 Hz and 200 Hz, were acquired by using a textile strap with a wearable sensor (Polar H10; Polar Electro OY, Kempele, Finland) placed under the chest. RR intervals with a resolution of 1 ms were provided separately. The signals and RR intervals were transferred to a smartphone with a mobile app in real-time via Bluetooth. To ensure a stable Bluetooth connection, the smartphone was placed in the holder wrapped around the upper arm of the patient. The smartphone was only taken out when a healthcare specialist logged the beginning of each test. A detailed description of the available data for each test is given in Fig. 2.1. A part of the signal database is accessible from *Physionet* [130].

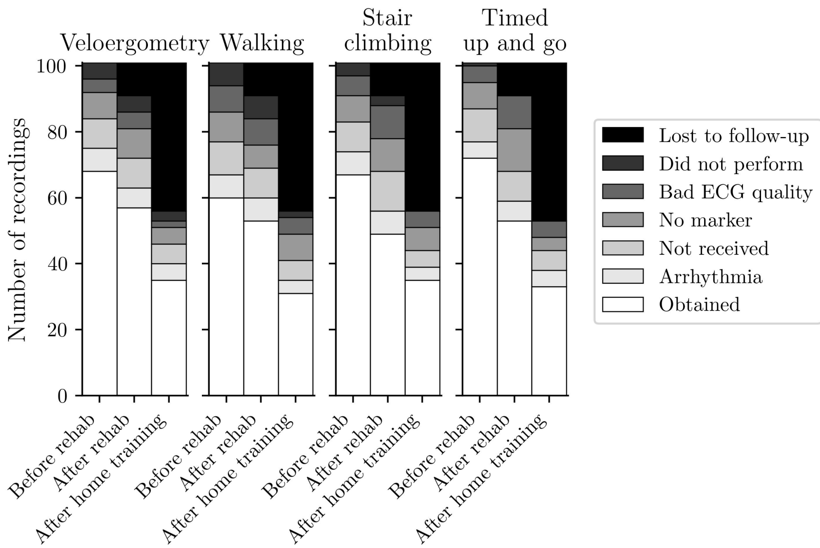


Figure 2.1. Data availability for each test. Here, 'lost to follow up' refers to patients who left the rehabilitation clinic earlier or did not return after home-based exercise training, 'did not perform' refers to tests that were not performed by the patients due to pain or any other reasons, 'bad ECG quality' refers to an unrecognizable electrocardiogram, 'no marker' refers to the absence of a marker indicating the onset of a test, 'not received' refers to the signals that were not received due to technical or user-related issues, 'arrhythmia' refers to atrial fibrillation, and 'obtained' refers to acquired good quality signals.

2.4. Exercise Training

All study participants attended inpatient rehabilitation consisting of patient education, diet counseling, psychological support, risk factor management, and individualized exercise training. The training duration and intensity were individually adapted based on the clinical and functional status. The inpatient exercise training program, described in detail in [131], includes light to moderate endurance training on a cycle ergometer (six sessions a week for up to 40 min depending on a patient's functional status), aerobic dynamic gymnastics in the sitting or/and standing position (five sessions a week for 30 min), resistance training focusing on lower limb muscles (three sessions a week for 15 min), balance training (three sessions a week for 15 min), and respiratory muscle training by using a lung exerciser (seven sessions a week for 15 min).

The home-based exercise training program included four different types of exercise:

- Aerobic endurance training (five sessions a week for 20–60 min, rate of perceived exertion 12–14). Walking, stair-climbing, and cycling of moderate to high intensity were recommended as proper physical activities.
- Sensomotoric training (three sessions a week for 15 min, rate of perceived exertion 11–12). Exercises on postural control, dynamic balance, and coordination of moderate to high intensity were advised.
- Resistance training (three sessions a week for 20–25 min, rate of perceived exertion 12–15). Four to eight exercises at moderate intensity, involving main muscle groups of the legs were proposed.
- Flexibility training (three sessions a week for 10–15 min, rate of perceived exertion 11–12). Isolated type flexibility exercises at low to moderate intensity, also including leg, arm, and neck stretching exercises, were offered.

All exercises were presented in easier and advanced versions so that the patients could choose from based on their health and functional status. To comprehend the home-based program, patients of the intervention group had three additional meetings with physiotherapists at the end of inpatient rehabilitation. The patients were provided with basic training equipment (e.g., stretch band, gymnastics ball, weights). To ensure proper participation in home exercise training, patients were inquired by phone every two weeks about adherence to the program.

2.5. Exercise Testing

Submaximal clinical tests, namely, 6-minute walking, stair-climbing, and timed up-and-go, were chosen as representatives of the common physical stressors in activities of daily living; the heart rate and acceleration signals of these activities are represented in Figure 2.2. Meanwhile, veloergometry was chosen as a maximal test for reference. Due to substantial effects on the patient's condition, veloergometry was performed on a different day than the submaximal tests. Before and after each test, a patient had to rest in a sitting position for at least three minutes. The tests were performed at the beginning of inpatient rehabilitation, after inpatient rehabilitation, and after home-based exercise training, see Figure 2.3.

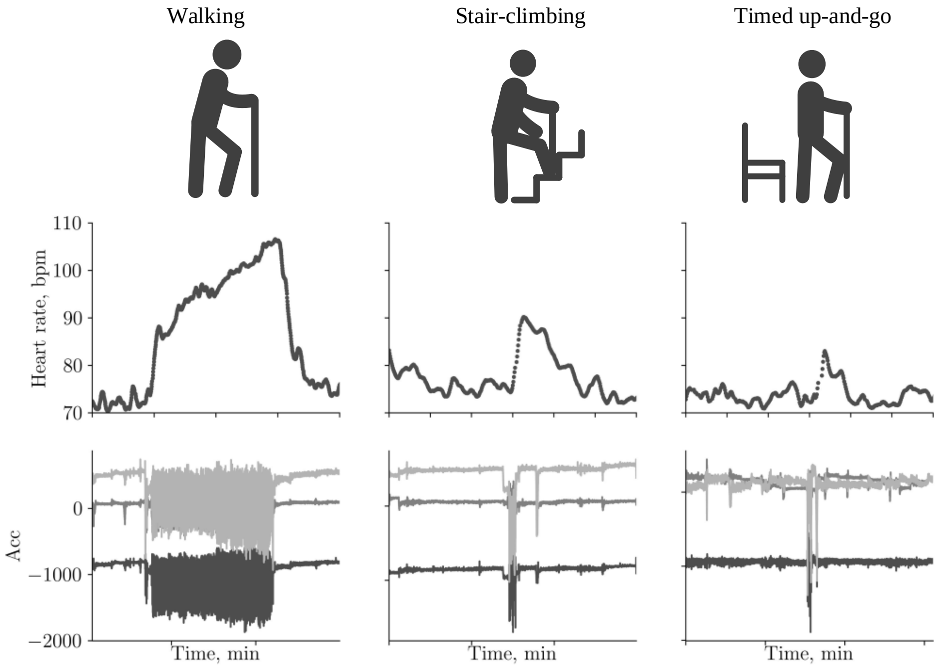


Figure 2.2. Heart rate and acceleration signals of walking, stair-climbing and timed up-and-go submaximal tests.

Veloergometry is a clinical standard for exercise testing used to evaluate the cardiovascular function under conditions of an increasing physical workload. Veloergometry was performed on a cycle ergometer *Viasprint 150P* (Ergoline GmbH, Germany) by using a ramp protocol starting at 25 watts and then increasing by 12.5 watts per minute until subjective exhaustion or occurrence of the termination criteria (dyspnoea, chest pain, leg fatigue, systolic blood pressure >220 mmHg, decrease in baseline systolic blood pressure >20 mmHg).

The 6-minute walk test is a well-established, safe, and inexpensive approach to assess the functional performance. The test was found to be beneficial in assessing the treatment efficiency across a variety of cardiopulmonary conditions [132]. The test does not demand maximal physical effort, hence it is accessible to most except for severely impaired older adults [133]. During the 6-minute walk test, the distance walked on a flat surface under the encouragement of a supervising staff member is judged based on the individual-specific reference distance.

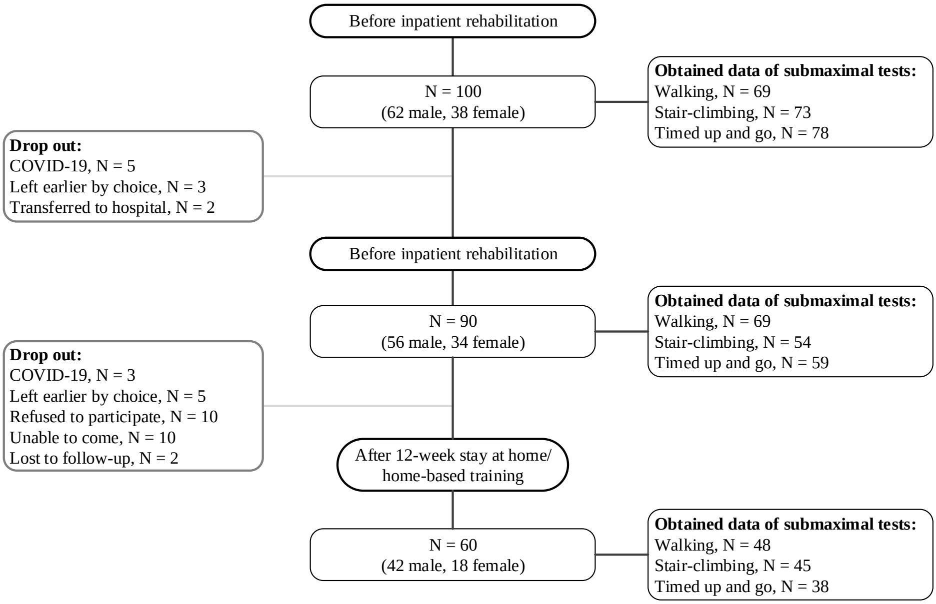


Figure 2.3. Patient enrollment flow diagram. Here N denotes the number of patients.

Stair-climbing was chosen assuming that terrain-dependent peculiarities may require additional physical effort compared to ordinary walking [134]. Stair-climbing has not yet been standardized for use in the clinical practice, thus the common approach is to instruct patients to climb the maximum number of stairs at a convenient pace [135]. Taking into account that frail patients after open-heart surgery are especially vulnerable, they were asked to climb only a set of 12 stairs at a convenient pace without assistance from a healthcare specialist and were allowed to terminate the test whenever they felt exhaustion, leg fatigue, or chest pain.

A timed up-and-go test was chosen due to assuming that the body position change may alter the HR response [136]. During the test, the patient is asked to change the body position from sitting to standing, walk 3 meters forward, turn around, and walk back to the chair to sit down.

2.6. Database-related Issues

Unfortunately, nearly one-third of our recordings were completely or partly lost due to various reasons, which resulted in a substantively reduced number of patients with available walk and stair-climbing tests. However, the effort required to record the data by using wearable devices should not be overlooked since data loss due to hardware, software, network, and user-related issues is a well-known problem [137, 138, 139] deserving transparency to mitigate the risk of similar issues in future studies. Patients had to perform various clinical tests over a 2–4 hour period; thus it was decided to turn on the devices at the beginning of the whole recording session and turn them off at the end. Despite the fact that monitoring was partly observed by healthcare specialists, most of the time, the patients' behavior, who were elderly and less familiar with technology, was unsupervised.

The custom-made software for signal acquisition crashed occasionally due to the following reasons: a patient walked too far from the data collecting smartphone when a healthcare specialist entered a time marker to indicate the beginning of the test, leading to the interrupted Bluetooth connection; a patient accidentally pressed a button on either the device or the smartphone; the device was not fully charged, and therefore discharged before the end of a monitoring session; the stable internet connection was occasionally unavailable due to maintenance or other reasons; a data transfer error occurred due to updates of the end-point server. The wearable device was also prone to stopping the sending of data during longer recording sessions, which sometimes happened even when the device was fully charged and with a stable Bluetooth connection. In addition, one-third of the patients were lost to follow-up and did not return to the clinic for assessment after home training.

2.7. Conclusions of the Chapter

1. The collected signals and clinical data have a wide range of potential applications, such as developing algorithms to assess frailty by using wearable devices, exploring new measures which reflect frailty, and investigating the relationships between clinical data, frailty status, and measures derived from biosignals.
2. Approximately one third of the collected data was unexpectedly lost due to technical and user-related issues, which emphasizes the importance of transparency and proactive solutions to address such challenges in future studies when wearable devices are utilized. Furthermore, the unsupervised behavior of elderly patients, coupled with a notable loss to follow-up, highlights the complexities associated with monitoring studies involving individuals who are unfamiliar with the particular technology.

3. METHODS

This chapter describes the developed approaches to improve the understanding of the effectiveness of exercise-based rehabilitation for patients with frailty. The approaches rely on the analysis of wearable-based biosignals, while specifically focusing on kinematic and HR response measures. The chapter also proposes a concept of an interpretable machine learning-based algorithm to identify clinically informative features which can provide valuable insights into an individual patient's frailty.

3.1. Detection of Physical Stressors

To distinguish between walking and stair-climbing, a derivative dynamic time warping algorithm was applied which nonlinearly assesses the similarity between the two time series, i.e., a signal under analysis and a template.

3.1.1. Preprocessing and templates of physical activity

Acceleration signals were filtered by using the 3rd order zero-phase Butterworth low-pass filter with a cut-off frequency of 15 Hz. The duration of walking was 6 min, whereas climbing one flight of stairs took from 10 to 20 s depending on the participant's functional status. Therefore, the analysis time interval was set to 10 s to cover both activities and was extracted from the middle of each activity in case the activity lasted longer. The extracted intervals were further used to manually detect three individual strides in the magnitude vector of the acceleration signal. To achieve a more accurate representation of the typical movement pattern and reduce the impact of potential outliers, the approach of selecting three strides from each participant was employed as visualized in Fig. 3.1 (a). The extraction of stride patterns was done manually to reduce the inaccuracies of automatic extraction. Since the subjects included in the study were frail, they often exhibited unusual movement patterns, thus the performance of already existing stride detection algorithms may introduce additional errors. The strides were resampled to 200 samples and averaged to create a representative activity for each participant. Finally, the templates for walking and stair-climbing were created by averaging the representative activities of all participants. The stair-climbing template was generated by utilizing 162 stride intervals extracted from 54 participants, whereas the walking template was generated based on 186 stride intervals extracted from 62 participants. To explore the effect of acceleration axes on the detection performance, the templates were found for anterior-posterior, mediolateral, and vertical axes, as well as for the magnitude vector. The stride intervals used for templates were later involved for classifying stair-climbing and walking by using the derivative dynamic time warping algorithm.

3.1.2. Derivative dynamic time warping-based algorithm

The similarity is assessed by finding the optimal warping path from signal X to template Y. The minimal distance $w_{i,j}$ is found by matching x_i samples to the samples y_j of template time series as visualized in Fig. 3.1 (b). The optimal distance W^* of the signal under analysis to the template is found by minimizing the path from (x_0,y_0) to (x_N,y_N), as shown in Fig. 3.1 (c):

$$W^* = \underset{W \in \mathbf{W}}{\arg\min}\ Dist_W(X, Y) \tag{3.1}$$

The signal under analysis is classified as either walking or stair-climbing, depending on which activity resulted in a lower W^* value.

Derivative dynamic time warping is a similarity assessment method which maps similar features between two time series. The advantage of this method is that features are recognized even when time series are not aligned or have different durations. Similarity is evaluated by calculating a cost function after aligning all of the data points.

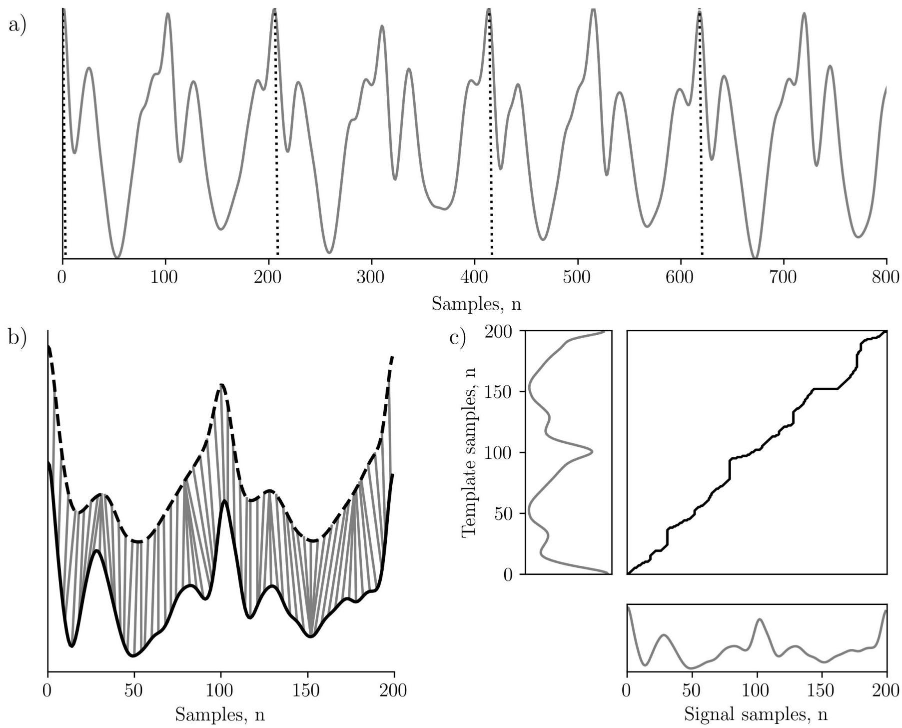


Figure 3.1. Template matching using a derivative dynamic time warping: a) extraction of strides from the acceleration signal, b) alignment of a signal under analysis (solid line) with the template (dashed line), and c) optimal alignment path.

$$D_x = \frac{(x_i - x_{i-1}) + ((x_{i+1} - x_{i-1})/2)}{2} \quad (3.2)$$

Fig. 3.2 illustrates the calculated distance for each participant during walking and stair-climbing by using the acceleration signal of the vertical axis.

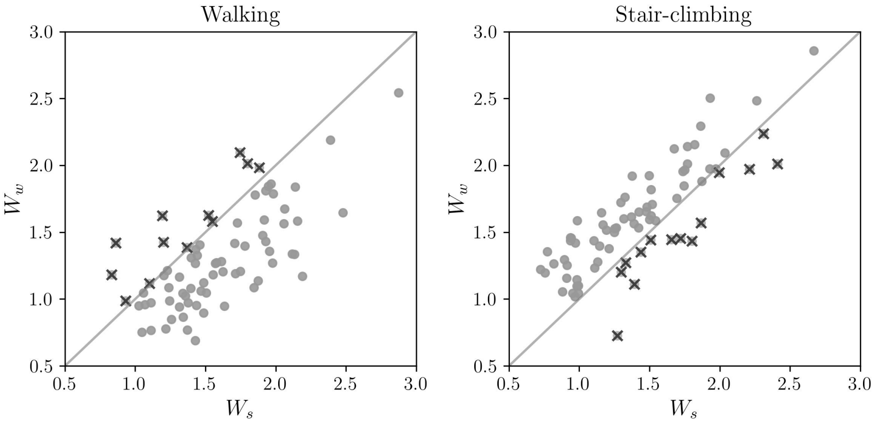


Figure 3.2. The distance of the signal under analysis from templates for walking and stair-climbing. Crossed dots represent incorrectly classified physical activity.

3.1.3. Performance evaluation

Detection performance was investigated in terms of sensitivity (Se) and the positive predictive value (PPV). Sensitivity involves the total number of a particular physical activity correctly detected as a particular activity, whereas the positive predictive value compares the number of the correctly detected particular activity to the total number of activities detected, including false detections.

3.2. Characterization of Kinematic Properties

3.2.1. Preprocessing of acceleration signals

There is a variety of measures suitable to describe kinematic properties [140], however, only those that can be estimated from a single sensor and provide different information about the gait and balance were considered. The kinematic measures were estimated from the triaxial acceleration signal which reflects movement in three axes, namely, vertical (Acc_V), mediolateral (Acc_M), and anterior-posterior (Acc_A), see Figure 3.3.

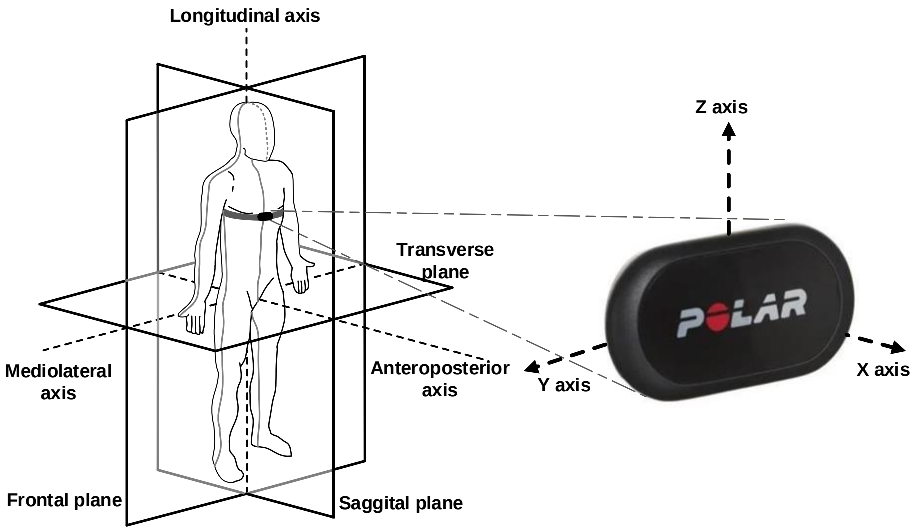


Figure 3.3. Presentation of the cardinal system representing axes and planes of the human body movement, and the positioning of Polar H10 device.

The acceleration signal consists of a static vertical gravitational component and a dynamic component due to velocity changes during motion. Therefore, the signal was preprocessed to mitigate the influence of these components. Prior to the estimation of all kinematic measures, the gravity component was removed by detrending the triaxial acceleration signal [134], whereas other preprocessing depended on the particular kinematic measures.

The stride time, cadence, and gait asymmetry were estimated based on the footsteps detected in the Acc_V signal filtered by using a third-order low-pass Butterworth filter with a cut-off frequency of 2.5 Hz [51]. Movement vigor was estimated in the raw triaxial accelerometer signal with a gravity component removed. Prior to the estimation of the Lissajous index and postural sway, slow body movements, such as due to respiration, were suppressed by using a third-order Butterworth high-pass filter with a cut-off frequency of 0.3 Hz, whereas electrical and mechanical noise was removed by using a third-order Savitzky–Golay smoothing filter with a frame length of 41 [46].

3.2.2. Estimation of kinematic measures

Many studies have shown that the stride time increases as frailty worsens [43, 47, 48, 51]. The stride time reflects the duration of the gait cycle and is defined as the time elapsed between the first contact of two consecutive footsteps of the same leg.

Frail adults often have reduced cadence, thus making this measure useful for the identification of pre-frailty [49, 141]. Cadence is expressed as the number of steps per minute during the analysis time period T.

The movement vigor directly affects the acceleration amplitude, thus, unsurprisingly, it was found to be powerful when discriminating between different intensities of physical activity [52, 142]. Since frail adults often move slower, this may result in a decreased movement vigor, here estimated as a mean amplitude deviation:

$$Vigor = \frac{1}{n}\sum_{i=1}^{n}\left|Acc(i) - \overline{Acc}\right|, \tag{3.3}$$

where $Acc(i)$ is the Euclidean sum of the samples of the triaxial acceleration signal, $\overline{Acc}$ is the mean value of Acc, and n is the number of samples during the analysis time period T.

Maintaining the gait symmetry in healthy people does not require considerable cognitive resources, however, cognitive effort may be needed to keep coordination under certain pathological states [50]. Since frailty affects the cognitive function [143], the gait may become more asymmetrical in increasingly frail patients due to the inability to cope with the additional cognitive input. Gait asymmetry, representing the left and right step coordination, is found by

$$Asymmetry = \frac{1}{k}\sum_{i=1}^{k}\frac{|t_l(i) - t_r(i)|}{t_l(i) + t_r(i)} \times 100, \tag{3.4}$$

where k is the number of strides over the analysis time period T, $t_l(i)$ and $t_r(i)$ are the left and right step times, respectively. A value of 0 reflects the perfect symmetry, whereas higher values show a greater degree of asymmetry.

The Lissajous index quantifies the movement symmetry in the mediolateral plane [56]. The Lissajous index is calculated by finding the difference between the areas of the rectangles enclosing the spaghetti plot obtained by plotting the acceleration signal in the vertical plane against the acceleration signal in the mediolateral plane (Fig. 3.4):

$$Lissajous\ index = 2\frac{|Area_p - Area_n|}{Area_p + Area_n} \times 100, \tag{3.5}$$

where $Area_p$ and $Area_n$ are the areas of the positive and negative sites of the rectangle-enclosed spaghetti plot, respectively. The Lissajous index of 0 shows the perfect movement symmetry, whereas it tends to increase for an increasing asymmetry.

A common approach to assessing balance is to estimate the postural sway [46, 144]. The postural sway is estimated based on the spaghetti plot obtained by plotting the acceleration signal in the anteroposterior plane against the acceleration signal in the mediolateral plane. The spaghetti plot is then enclosed by using a convex hull approach which finds the smallest convex polygon that wraps all data points. The total area of the convex hull is defined as the postural sway (Fig. 3.4).

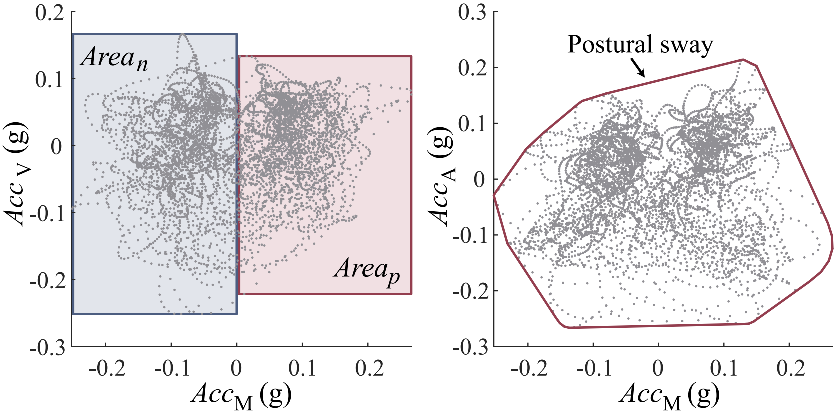


Figure 3.4. A spaghetti plot of acceleration signals in the vertical and the mediolateral planes, enclosed by rectangles, used to calculate the Lissajous index (left). The convex hull of the spaghetti plot of acceleration signals in the anteroposterior and the mediolateral planes was used to estimate the postural sway which is equal to the sway area (right).

All kinematic measures described above were extracted both during walking and stair-climbing. The analysis time period T was set to 30 s for the walk test. To better represent steady walking, the onset of the analysis time window was chosen to be 30 s after the beginning of the walk test assuming that cadence tends to be more variable at the beginning of the test. This assumption is substantiated by the observation that the distance walked during the 6-min walk test slightly declines after the first 2 min and remains stable afterwards [145]. Based on this finding, an alternative possibility was to set the beginning of the analysis time interval after the 2-min datapoint. However, walking bouts of a longer duration might be too exhausting for severely frail adults, which would result in slowdowns or stops. This reasoning can be supported by a study showing that unintentional walk tests of 2-min duration are nearly twice as common as 6-min among elderly patients with cardiovascular disease [53]. Since ascending the stairs was challenging for some patients, as this resulted in stops or early termination, T was set to 10 s. The beginning of the stair-climbing test defined the onset of the analysis time window.

3.2.3. Performance evaluation

Either walk or the stair-climbing test was unavailable for some patients due to various reasons, which resulted in an unequal number of patients with completed tests for a particular analysis. The Shapiro-Wilk test was used to assess the data normality, and because of the non-normal distribution, the nonparametric tests were used to compute the p-values. Statistical significance was set at $p < 0.05$.

Kinematic and functional capacity measures before and after inpatient rehabilitation are represented by boxplots. Only patients with available walking and stair-climbing tests both before and after inpatient rehabilitation were included in the analysis. The Wilcoxon signed-rank test was applied to compute the p-values for the differences between dependent groups.

Kinematic and functional capacity measures before and after home-based exercise training/stay at home in intervention and control groups are given as a mean and a standard deviation. Only those patients with available walking and stair-climbing tests both before and after home-based exercise training/stay at home were included in the analysis. The Mann–Whitney U test was applied to compute the p-values for the differences between independent groups.

Kinematic and functional capacity measures in the groups of non-frail (EFS: 0–3), vulnerable (EFS: 4–5), and frail (EFS: $\geqslant$6) participants are represented as a mean and a standard deviation. For this analysis, the kinematic measures were estimated after inpatient rehabilitation whenever data was available. When data was unavailable after inpatient rehabilitation, data from the beginning of rehabilitation was used instead. The Kruskal–Wallis H-test was applied to compute the p-values for the differences among independent groups.

3.3. Characterization of Heart Rate Response

3.3.1. Biosignal preprocessing

Before HR characterization, RR series were processed to ensure that only normal-to-normal intervals were included for analysis. Atypical RR intervals which include missed, extra, and ectopic beats were corrected by analyzing successive RR interval differences by using the algorithm described in [146]. Extra beats were corrected by removing the corresponding beats, whereas new beats were added in place of the missing beats so that the long RR interval could be divided into two halves. Ectopic beats were corrected by interpolating the corresponding RR intervals. Additionally, all corrected RR series were manually inspected by analyzing a synchronously recorded electrocardiogram.

Estimation of the HR response measures requires the detection of the peak HR and HR recovery onset. The peak HR rate is the maximal HR during the entire HR response phase. Detection of the recovery onset immediately after the cessation of physical activity is explained in detail in our previous work [70]. Briefly, search for the recovery onset is performed by fitting a line to the HR series in a sliding window of 1 min. Then, the time interval with the steepest falling slope is chosen as a suspected recovery phase. The HR series 25 s before and 25 s after the beginning of the steepest falling curve is taken for fitting a polynomial curve where the maximal value determines the onset of the recovery phase, see Figure 3.5.

Baseline HR measures were estimated from a resting phase of 3-minute duration before the exercise test. To ensure that the measures are not altered by movements,

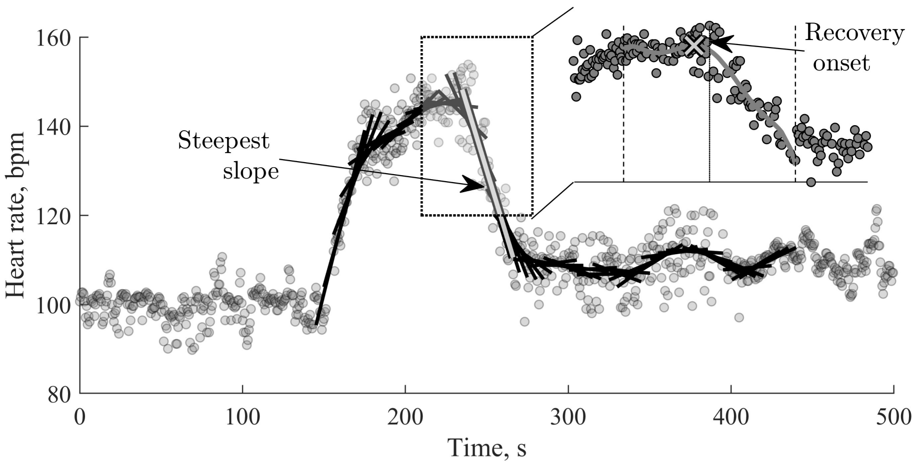


Figure 3.5. Exemplary illustrations of detection of the peak HR and HR recovery onset.

the rest phase with a less intense activity, as measured by the triaxial accelerometer, is chosen as the most representative point.

3.3.2. Exclusion of heart rate series

HR series unacceptable for the estimation of measures, i.e., showing no HR response to the physical activity or exhibiting a high HR variation during the recovery phase, were excluded from the analysis. No response to an exercise test was considered when HR did not rise at least 5 bpm above the average baseline HR. HR variations either caused by physiological factors or by unexpected activity (e.g., turning or leaning) were considered unacceptable when exponential fitting to the recovery phase, determined via the coefficient of determination R^2, was below the fixed threshold of 0.5 [70]. Examples of typical and unacceptable HR series for each type of exercise test are given in Fig. 3.6.

3.3.3. Heart rate response measures

To comprehensively characterize the HR response, the measures covering the accelerating phase, decelerating phase, and the entire HR response were chosen for investigation.

The accelerating phase of HR response is characterized by the time interval T_a during which HR accelerates until it reaches the peak HR (HR_p) starting at the onset of a particular exercise test [63]. The time to peak HR was found to be prolonged in frail older adults compared to non-frail adults during walking [63].

The decelerating phase of the HR response is characterized by post-exercise HR recovery which reflects the capacity to respond and adapt to the maximal or submaximal physical activity [64]. The fast recovery phase is characterized by the short-term

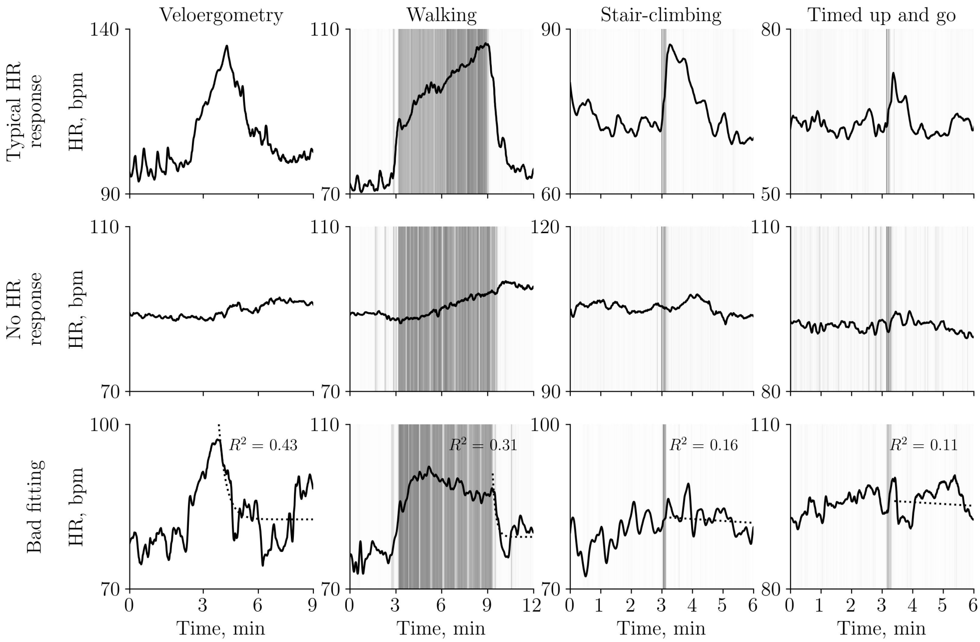


Figure 3.6. Exemplary illustrations of typical and unacceptable HR series for the estimation of measures during veloergometry and submaximal tests. Grey bars indicate the physical activity intensity estimated as a mean absolute deviation of the triaxial acceleration signal. Physical activity intensity cannot be estimated during veloergometry due to sitting on the cycle ergometer.

time constant (T_{30}) which is found by fitting the line of 30 s duration to the logarithm of HR, where T_{30} is the negative inverse of the slope of the resulting line. To improve reproducibility, T_{30} is estimated within the first min after the recovery onset in a sliding window of 30 s, and the lowest value is selected [147]. Meanwhile, the slow recovery phase is characterized by a decay of HR at 120 seconds (HRR_{120}) after the recovery onset. A slower HR recovery may indicate cardiac autonomic dysfunction, and it was found to be associated with a broad range of cardiovascular diseases and an increased risk of mortality [64].

The entire HR response is characterized by the HR reserve which is a measure of chronotropic competence independent of age, resting HR, and physical fitness [148]. The HR reserve is found by

$$RES = \frac{HR_{\mathrm{p}} - HR_{\mathrm{r}}}{HR_{\mathrm{a}} - HR_{\mathrm{r}}} \times 100, \tag{3.6}$$

where HR_{r} is a resting HR derived from the resting period before the exercise test, and HR_{a} is the attainable HR calculated as 220 minus age in years.

Low RES may indicate an impaired chronotropic response, whereas it is roughly 100% in healthy people during peak exercise.

3.3.4. Characterization of baseline heart rate

Elevated resting HR, reduced HR complexity, and reduced HR variability indicate autonomic imbalance manifesting as an increased sympathetic and/or decreased parasympathetic tone [62].

Resting HR (HR_{r}) is calculated as an average HR over the entire resting phase prior to the exercise test. An elevated resting HR is an established independent risk factor for all-cause and cardiovascular mortality [149], and it was also found to be higher among frail older adults compared to non-frail individuals [136].

The HR complexity during rest prior to exercise is assessed by using sample entropy (SampEn) [60, 150]. Given the HR pattern length m and the similarity threshold η showing the tolerance for accepting similar patterns, the sample entropy estimates the logarithmic probability of similar m-length patterns to remain similar for $m + 1$ [150]. Sample entropy is close to 0 for regular HR, whereas it takes larger values for unpredictable HR. In this study, η was set to 0.15, and m was set to 2 as in [60]. Reduced HR complexity may indicate autonomic dysfunction in people with frailty.

To assess ultra-short-term HR variability [151], the standard deviation of all normal-to-normal RR intervals (SDNN) during rest before the exercise test is computed. Reduced SDNN may indicate a decreased parasympathetic activity in frail adults [60].

Characterization of the HR response and baseline HR is illustrated in Fig. 3.7.

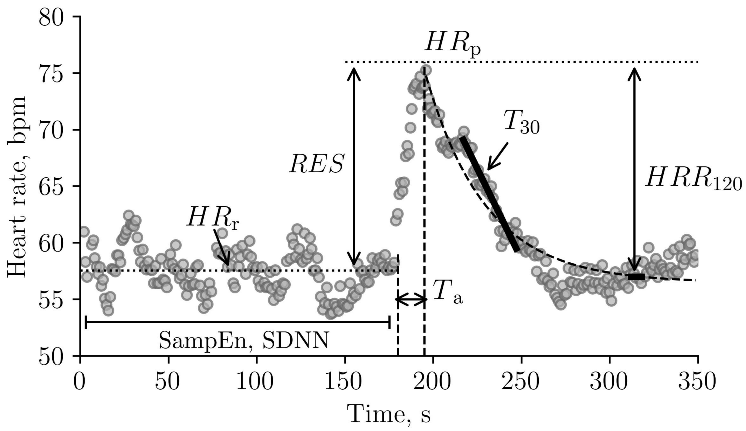


Figure 3.7. Characterization of baseline HR and HR response. Note that RES also involves normalization by [(200 – age) – HR_{r}]. The onset and the cessation of physical activity are at 180 s and 195 s, respectively.

3.3.5. Performance evaluation

Some veloergometry, walking, stair-climbing, and timed up-and-go tests were unavailable, which resulted in an unequal number of patients with completed tests for a particular analysis.

The agreement between the HR response to veloergometry and submaximal tests is expressed as the mean difference and 95% confidence interval. Associations between the HR response to veloergometry and each submaximal test are represented by scatter plots. The relationship is assessed by using linear regression and given as the Pearson correlation coefficient.

To assess the relationship between HR measures and the frailty status, the HR response and baseline values of HR measures are subdivided into quartiles. The corresponding EFS values of each quartile are given as the mean and standard deviation. The Shapiro-Wilk test was used to assess data normality, and, because of non-normal distribution, the nonparametric Kruskal-Wallis H-test was used to calculate the p-value for the differences between the EFS values of the corresponding quartiles.

To investigate the effect of inpatient cardiac rehabilitation on the HR response measures, only patients with available tests both before and after inpatient rehabilitation were included in the analysis. In the case of a normal distribution, the Student t-test for paired data was applied to calculate the p-value. Otherwise, the Wilcoxon signed-rank test was used.

The effect of the entire exercise training program, covering inpatient cardiac rehabilitation and home-based training, is expressed as the mean and standard deviation. HR response measures were estimated after home-based training and before inpatient rehabilitation whenever data was available. When data was unavailable, the data recorded after inpatient rehabilitation was used instead. In the case of a normal distribution, the Student t-test for paired data was used to calculate the p-value for the change of measures within the intervention and control groups. Otherwise, the Wilcoxon signed-rank test was applied. Meanwhile, the differences in the change of values before and after the entire exercise training program between the intervention and control groups were assessed by using the Student t-test for unpaired data in the case of a normal distribution. Otherwise, the Mann–Whitney U test was applied.

3.4. Identification of Frail Physiological Functions

3.4.1. Frailty components under analysis

The frailty status can be influenced by various components, including physical, cognitive, social, and psychological factors [152]. Although physical components are often prioritized in clinical evaluations, it is important to develop approaches which accurately identify the frailest component among others. Social, mental and clinical components are usually either slow-changing (cognition, medication use), unreliable (mood) or can be assessed only by a patient (continence, social support). Therefore, only physical components, namely, general health status, functional independence, nutrition, and functional capacity of the EFS were analyzed, see Table 3.1.

Table 3.1. EFS components and respective ranges. The components chosen for investigation are bolded.

Component	Range	Type
Cognition	0 - 2	Mental
General health status	0 - 2	**Physical**
Functional independence	0 - 2	**Physical**
Social support	0 - 2	Social
Medication use	0 - 1	Clinical
Nutrition	0 - 1	**Physical**
Mood	0 - 1	Mental
Continence	0 - 1	Clinical
Functional performance	0 - 2	**Physical**

3.4.2. Features for machine learning model

The relevant features which characterize physiological functions (i.e., gait, balance, HR response) are selected based on their association with frailty and ability to characterize different components. Two sets of features were chosen for investigation: those obtained from wearable devices and from clinical equipment for a reference.

Wearable-based features characterizing the gait include the number of steps, cadence, gait irregularity, and movement vigor. The balance features include gait asymmetry, postural sway, sway irregularity, and Lissajous index. The HR response features include HRR_{60}, HRR_{120}, T_{30}, RES, HR_p, and T_a. All of these measures are extracted from the walking and stair-climbing activities.

Clinical features characterizing the gait are the timed up-and-go score, the distance walked during the 6-minute walk test ($6MWD$), and the gait speed. The balance features include the step width, gait asymmetry, double support percentage, and the center of pressure (CoP) length variability, evaluated by the Zebris gait and stance analysis system. The HR response features include HRR_{60}, HRR_{120}, RES, T_{30}, HR_{max} and T_a obtained during veloergometry.

In addition, the age, body mass index, and days after the heart surgery were included for both sets of features.

3.4.3. Machine learning model

Due to a large number of features and a small number of samples, the decision trees model was chosen to classify EFS components. The decision tree is a tree-like model that is used to make decisions based on the values of features and their corresponding outcomes. In the binary classification, the decision tree is used to classify data into one of two categories.

The decision trees model finds an optimal threshold of each of the most important features to group the samples, thus minimizing the prediction error. The tree is constructed by recursively splitting the data into smaller subsets based on the values of the features. The split is done in a way that minimizes the impurity of the resulting subsets.

The impurity of a subset is measured by the information gain metric which measures the reduction in entropy of the samples representing each label in the subset after the split. The splitting process continues until a stopping criterion has been met, such as reaching a maximum depth or a minimum number of samples in a leaf node. At this point, the decision tree is considered trained and can be used to clasify new data. To classify new data, the features of the data are evaluated against the decision tree, by following the path from the root node to a leaf node. The leaf node reached by following the path represents the predicted class of the data. To improve the predictive capabilities of decision trees, the ensemble algorithm of gradient boosting is adapted. The structure of the proposed algorithm is presented in Figure 3.8 [153].

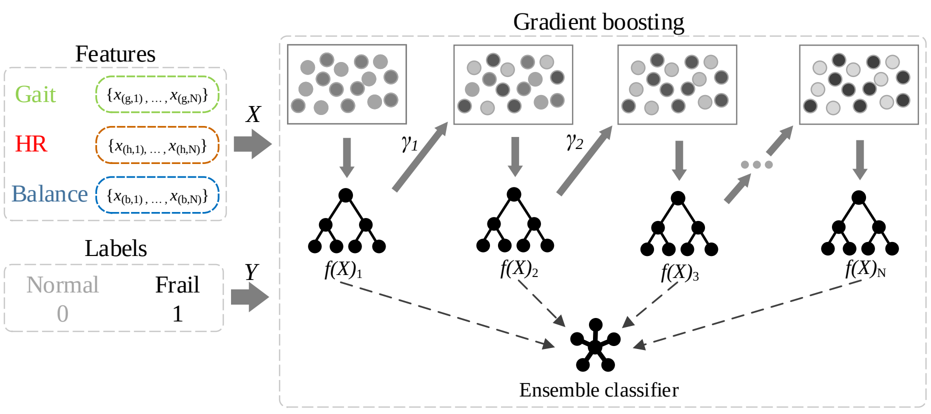


Figure 3.8. Structure of gradient-boosting decision trees model.

The primary decision trees model is constructed by fitting the actual values of samples, namely, either normal (0) or frail (1). The gradient boosting method is based on the iterative generation of weak decision trees models. However, each iteration is constructed by fitting the residuals γ of the previous prediction from the actual values. At the end of the process, the models are combined to form a final prediction model that is more accurate than any of the individual models. During the training process, the algorithm applies a loss function to determine the difference between the predicted values and the actual values. The gradient of this loss function is then utilized to modify the model parameters with the aim of minimizing the error. The gradient boosting ensemble model is used for its ability to learn non-linear relationships between variables. In addition to the improvement of accuracy, gradient boosting also reduces the risk of over-fitting.

3.4.4. Interpretation of model classifications

The EFS represents different characteristics of health condition; thus, different features are expected to be more important when classifying each component [154]. To determine the importance of individual features, the permutation feature importance method is applied [155].

The importance of parameter j is calculated by comparing the error of the original model e^o and the model with with permuted values e^p:

$$e^o = L(y, f(X)), \tag{3.7}$$

$$e^p = L(y, f(X^p)), \tag{3.8}$$

where X is the collection of features, and y is a label (normal or frail). Feature importance FI_j represents the reduction of the classification error when the value of the feature is removed, via permutation of the feature vector.

$$FI_j = \frac{e^{orig}}{e_j^p}, \tag{3.9}$$

FI of a particular EFS component is calculated as a sum of features representing that function.

For the interpretation of individual predictions, the Shapley additive explanations method (SHAP) is used. SHAP indicates an average additive change in classification when the feature is considered in the model. The importance of feature j is estimated by calculating the additive predictive value ϕ for every iteration of m, when m = 1,...,M. Iterations consist of all possible combinations of X features.

$$\phi_j^m = f(X_{+j}^m) - f(X_{-j}^m), \tag{3.10}$$

where X_{+j} and X_{-j} indicate models constructed with and without feature j. The average of the predictive value of all iterations is the SHAP value.

$$\phi_j = \frac{1}{M}\sum_{m=1}^{M} \phi_j^m. \tag{3.11}$$

The SHAP of a particular physiological function is calculated as a sum of the SHAP values calculated for the features which characterize that function.

3.4.5. Performance evaluation

To evaluate the accuracy of the regression models, a leave-one-out cross-validation was employed, where the model was tested on the data of each participant and trained on the remaining dataset. The performance of the models was assessed by finding their classification accuracy, specifically for each of the four EFS components, by determining whether they were weakened or normal.

Since the accuracy of the models is dependent on the appropriate selection of the training hyperparameters, such as the number of estimators (N), the maximum depth of the decision tree (h), and the learning rate (l), the best combination of training hyperparameters was found by testing the accuracy of the models by using various hyperparameter combinations. The performance of the model was evaluated by using F_1 score (Eq. 3.12):

$$F_1 = \frac{TP}{TP + \frac{1}{2}(FP + FN)}, \tag{3.12}$$

where TP, FP, and FN are true positive, false positive, and false negative clasifications, respectively.

3.5. Conclusions of the Chapter

1. The derivative dynamic time warping-based algorithm has been proposed to detect physical stressors in wearable-based biosignals, with a focus on walking and stair-climbing as these activities are feasible even among frail individuals.
2. Gait and balance measures were chosen to investigate the potential of using kinematic measures extracted from the acceleration signals of a single wearable sensor to track the frailty trajectories during exercise training.
3. To comprehensively assess the heart rate response to physical stressors, it has been proposed to utilize measures encompassing the acceleration phase, deceleration phase, and the overall heart rate response.
4. A concept of interpretable machine learning has been proposed for identifying clinically informative features that provide information on the frail physiological functions of an individual patient.

4. RESULTS

This chapter presents the findings regarding the detection of physical stressors, the assessment of the kinematic and HR response measures, and the results of an interpretable machine learning-based algorithm for identifying the frailest components. These findings contribute to a better understanding of frailty assessment and highlight the potential of wearable-based approaches in monitoring frail patients.

4.1. Detection of Physical Stressors

The performance of a derivative dynamic time warping-based algorithm for acceleration signals of anterior-posterior, mediolateral, and vertical axes, as well as for the magnitude vector of acceleration is given in Table 4.1. The best overall performance is achieved when using the acceleration signal of the vertical axis, which results in Se of 84.2$\%$ and PPV of 82.1$\%$ for detecting walking and Se of 81.6$\%$ and PPV of 83.8$\%$ for detecting stair-climbing scores.

Table 4.1. The performance of a derivative dynamic time warping-based algorithm.

	Walking		Stair-climbing		
	$Se, \%$	$PPV, \%$	$Se, \%$	$PPV, \%$	ACC
Anterior-posterior	95.1	69.5	57.9	93.6	76.9
Mediolateral	75.0	68.7	65.8	72.5	70.4
Vertical	84.2	82.1	81.6	83.8	82.9
Magnitude vector	97.4	65.5	46.7	94.9	73.0

Table 4.2 presents the performance for the groups of frail (EFS <6 points) and vulnerable/non-frail (EFS $\geqslant$6 points) participants when using an acceleration signal of the vertical axis. The results show that the algorithm is more sensitive (Se = 86.9$\%$) when detecting walking in frail adults compared to stair-climbing (Se = 79.1$\%$). The opposite tendency is observed for the vulnerable/non-frail group.

Table 4.2. The performance in the groups of different frailty statuses.

	Walking		Stair-climbing		
	$Se, \%$	$PPV, \%$	$Se, \%$	$PPV, \%$	ACC
Frail	86.9	81.6	79.1	85.0	82.5
Vulnerable/non-frail	80.0	82.8	84.9	82.4	83.2

Discussion. This study explored the feasibility of detecting physical stressors in adults with frailty, which is a challenging issue due to the weakness and slowness of these persons, which results in an inconsistent speed and intensity of physical activities. The proposed derivative dynamic time warping-based algorithm allows to mitigate the influence of inconsistent movements by aligning acceleration signals non-linearly. The ability to detect physical stressors, such as walking and stair-climbing, in daily living opens up the possibility to provide additional measures about the physiological reserve of frail adults.

Previous studies indicate that people with frailty suffer from increased fatigue and a higher risk of falling. These findings explain additional issues associated with the detection of physical stressors in adults with frailty. Walking, and especially more physically demanding activities such as stair-climbing, tend to be less consistent, often with slowdowns and stops. Additionally, pain in the lower extremities or torso can induce asymmetry of consecutive steps, which further complicates the detection of physical stressors in acceleration signals [156]. These peculiarities hinder the performance of template-matching methods relying on correlation between the signal under analysis and the template.

The limitation is that only two types of activities were considered for detection. The main motivation for choosing walking and stair-climbing was that these activities are common in daily living, including most adults with frailty. However, considering the application of the proposed algorithm in daily life, accounting for alternative activity types, such as riding a bicycle, will be necessary.

4.2. Frailty Kinematic Measures

4.2.1. Effect of inpatient rehabilitation

Forty-eight patients underwent available walk tests before and after inpatient rehabilitation, and their EFS scores dropped from 6.0 to 4.7, on average. Three patients improved their EFS scores by four points, six by three, nine by two, and 17 by one point after inpatient rehabilitation. The scores did not improve in 11 patients, and deteriorated by one in two patients. The performance in veloergometry, 6-min walk, and timed up and go tests improved from 52.1 $\pm$ 18.3 W to 61.3 $\pm$ 19.2 W ($p < 0.001$), from 301.1 $\pm$ 79.4 m to 387.2 $\pm$ 83.8 m ($p < 0.001$), and from 8.3 $\pm$ 2.2 s to 7.6 $\pm$ 1.7 s ($p = 0.017$), respectively. Fig. 4.1 shows that all kinematic measures, except for gait asymmetry and the Lissajous index, improved considerably during walking for most patients after inpatient rehabilitation ($p < 0.001$). That is, the stride time decreased in 34 (71%) patients, cadence increased in 37 (77%), movement vigor increased in 40 (83%), and postural sway increased in 39 research subjects (81%). An increase in postural sway can be explained by a wider range of motion due to the better overall physical condition after open-heart surgery.

Forty-four patients underwent available stair-climbing tests before and after inpatient rehabilitation, and their EFS score dropped from 6.1 to 4.6, on average. One patient improved the EFS scores by six, one by five, three by four, four by three, eight by two, and 15 by one. The scores did not improve in 12 patients. The performance in veloergometry, 6-min walk, and timed up and go tests improved from 51.2 $\pm$ 16.3 W to 62.0 $\pm$ 17.7 W ($p < 0.001$), from 298.7 $\pm$ 77.2 m to 380.9 $\pm$ 89.8 m ($p < 0.001$), and from 8.4 $\pm$ 2.0 s to 7.5 $\pm$ 1.8 s ($p = 0.008$), respectively. The kinematic measures during stair-climbing improved to a lesser extent compared to walking (Fig. 4.1). The stride time decreased in 32 (73%) ($p < 0.001$), cadence increased in 25 individuals (57%) ($p = 0.003$), and movement vigor increased in 28 (64%) ($p = 0.009$).

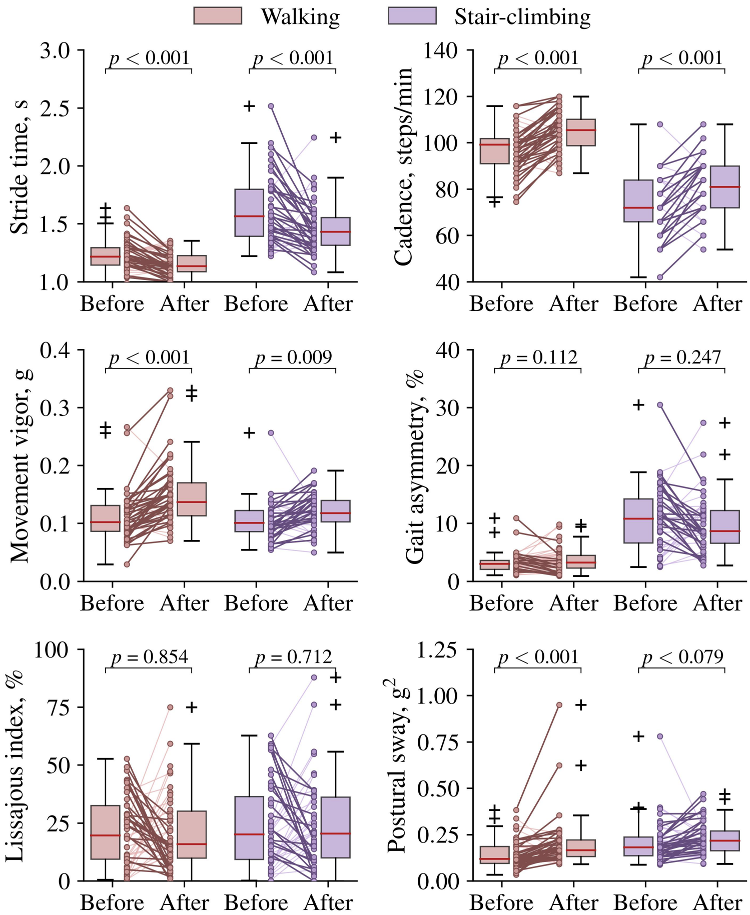


Figure 4.1. Kinematic measures estimated during the walk and stair-climbing tests before and after inpatient rehabilitation. A trend towards improvement in kinematic measures is depicted by the thicker line.

Discussion. Balance-reflecting measures are usually estimated during quiet standing either with open or closed eyes [127]. Given the far-reaching aim of our study to assess the kinematic response to the common daily life activities, quiet standing was not viewed as a suitable activity, especially considering the potential difficulties in reliably detecting quiet standing while using a wearable device. Contrary to the observation in [43], reporting a positive relationship between higher postural sway values and a worse frailty status, the present study showed the reverse, namely, an increase in the postural sway after inpatient rehabilitation. This finding can be explained by the healing of the surgical site and an improved patient mobility.

Kinematic measures were estimated during supervised clinical tests, therefore, scores may differ when obtained during causal walking and stair-climbing. A recent surgery, clinical environment, and guidance by healthcare specialists may have influenced the patients' motivation and the pace at which the tests were performed. In addition to that, an improvement in kinematic measures throughout inpatient rehabilitation may have been affected by the learning effect bias. Due to the learning effect, the performance on clinician-administered walk tests tends to improve in successive tests and can result in up to 14% increase in the distance walked [157]. This can be a major factor causing a high variability in distance during clinician-administered walk tests [158]. Unintentional walk testing, described in detail in [53], should be less affected by learning since it depends on the functional status rather than on familiarity with the test.

Parts of Sec. 4.2.1 have been quoted verbatim from the previously published article [17]

4.2.2. Effect of home-based exercise training

No difference is reflected by most kinematic measures between the intervention and the control groups before and after home-based training/stay at home, which corresponds to the absence of difference in the EFS scores, see Table 4.3. The EFS score slightly increased in both groups, which indicates that unsupervised reduced intensity exercise training did not result in a further improvement of the frailty status. Somewhat unexpectedly, the Lissajous index increased by 13.1% in the intervention group and decreased by 5.14% in the control group ($p = 0.021$), which suggests larger movement asymmetry among those who continued training. During stair-climbing, the movement vigor increased by 0.01 g in the intervention group and by 0.03 g in the control group ($p = 0.046$).

Discussion. For this study, the program was prepared by the clinic's physiotherapist taking into account frailty-caused restrictions to exercise training. Somewhat unexpectedly, no further improvement in the intervention group, instructed to continue exercising at home, was observed compared to the controls, despite the sudden improvement of both groups after inpatient rehabilitation. While the explanation for no difference between the intervention and control groups is not obvious, the three further months of unsupervised training at reduced intensity probably did not influence

Table 4.3. Changes in kinematic and functional capacity measures in the intervention group who performed the home-based exercise training program and controls who were asked to maintain their usual physical activity regimen.

	Walking		
	Intervention (N = 18)	Control (N = 11)	p-value
Stride time, s	-0.02 ± 0.17	-0.12 ± 0.21	0.342
Cadence, steps/min	5.24 ± 9.70	7.45 ± 12.0	0.854
Movement vigor, g	0.03 ± 0.07	0.05 ± 0.06	0.538
Gait asymmetry, %	0.75 ± 3.81	-1.06 ± 3.26	0.129
Lissajous index, %	13.1 ± 19.7	-5.14 ± 23.6	**0.021**
Postural sway, g^2	0.07 ± 0.16	0.07 ± 0.09	0.582
Peak workload, W	7.07 ± 10.4	10.8 ± 7.82	0.205
6-min walk distance, m	34.7 ± 84.5	49.3 ± 81.9	0.677
Timed up-and-go duration, s	0.97 ± 2.96	0.71 ± 2.15	0.524
EFS score	0.47 ± 1.77	0.00 ± 1.97	0.520
	Stair-climbing		
	Intervention (N = 15)	Control (N = 20)	p-value
Stride time, s	-0.04 ± 0.17	-0.07 ± 0.22	0.590
Cadence, steps/min	1.67 ± 10.0	-3.27 ± 8.64	0.204
Movement vigor, g	0.01 ± 0.04	0.03 ± 0.02	**0.046**
Gait asymmetry, %	0.21 ± 4.59	-2.47 ± 8.48	0.982
Lissajous index, %	-0.55 ± 24.5	-3.63 ± 30.0	0.840
Postural sway, g^2	0.04 ± 0.06	-0.01 ± 0.07	0.051
Peak workload, W	6.00 ± 9.65	12.2 ± 10.0	0.149
6-min walk distance, m	34.3 ± 70.4	39.9 ± 65.2	0.916
Timed up-and-go duration, s	1.12 ± 2.63	0.88 ± 1.87	0.782
EFS score	0.39 ± 1.72	0.27 ± 2.10	0.891

N denotes the number of patients in a particular group.
Certain parameter values are given as mean ± standard deviation.

the kinematic measures to such an extent as that observed during supervised inpatient rehabilitation. Furthermore, it cannot be ruled out that some patients in the control group changed their physical activity habits and started exercising after completing inpatient rehabilitation. Another factor hiding the differences may be that at least one-third of the patients in the intervention group did not exercise regularly as was revealed during phone interviews.

Parts of Sec. 4.2.2 have been quoted verbatim from the previously published article [17]

4.2.3. Kinematic and functional capacity measures for different frailty status

Table 4.4 shows kinematic measures when patients are grouped into non-frail, vulnerable, and frail groups according to their EFS scores. In general, the groups of different frailty statuses can hardly be distinguished based on the kinematic measures under in-

Table 4.4. Kinematic and functional capacity measures estimated during the walk and stair-climbing tests after inpatient rehabilitation within the groups of different frailty statuses.

	Walking			
	Non-frail (N = 18)	Vulnerable (N = 40)	Frail (N = 32)	p-value
Stride time, s	1.20 ± 0.22	1.19 ± 0.14	1.24 ± 0.16	0.166
Cadence, steps/min	103.1 ± 13.7	101.8 ± 11.2	97.6 ± 11.7	0.083
Movement vigor, g	0.16 ± 0.06	0.13 ± 0.05	0.12 ± 0.06	**0.005**
Gait asymmetry, %	4.02 ± 3.40	3.75 ± 2.40	4.12 ± 3.20	0.918
Lissajous index, %	20.6 ± 13.3	21.4 ± 15.0	22.5 ± 17.1	0.976
Postural sway, g^2	0.24 ± 0.21	0.16 ± 0.06	0.15 ± 0.06	**0.048**
Peak workload, W	64.9 ± 22.9	62.6 ± 23.2	53.5 ± 15.3	0.147
6-min walk distance, m	416.4 ± 87.2	366.9 ± 112.4	322.4 ± 83.9	**0.002**
Timed up-and-go duration, s	7.00 ± 1.18	7.75 ± 1.50	8.92 ± 2.19	**0.004**
EFS score	2.56 ± 0.62	4.45 ± 0.50	7.34 ± 1.18	<**0.001**
	Stair-climbing			
	Non-frail (N = 16)	Vulnerable (N = 32)	Frail (N = 35)	p-value
Stride time, s	1.46 ± 0.27	1.54 ± 0.27	1.64 ± 0.35	0.143
Cadence, steps/min	82.1 ± 12.1	77.6 ± 12.6	73.2 ± 13.4	0.097
Movement vigor, g	0.12 ± 0.04	0.11 ± 0.03	0.11 ± 0.04	0.384
Gait asymmetry, %	9.33 ± 4.51	10.4 ± 4.91	10.8 ± 5.31	0.648
Lissajous index, %	22.2 ± 21.4	25.8 ± 21.7	23.8 ± 14.6	0.675
Postural sway, g^2	0.23 ± 0.08	0.21 ± 0.08	0.20 ± 0.09	0.268
Peak workload, W	65.3 ± 19.8	61.3 ± 19.5	52.7 ± 15.3	**0.047**
6-min walk distance, m	402.6 ± 76.7	359.1 ± 97.9	313.0 ± 85.7	**0.002**
Timed up-and-go duration, s	6.78 ± 0.98	7.78 ± 1.65	9.14 ± 2.80	**0.002**
EFS score	2.69 ± 0.48	4.34 ± 0.48	7.11 ± 1.13	<**0.001**

Patients are classified into three categories based on the EFS score: non-frail (0–3 points), vulnerable (4–5 points), and frail (⩾6 points) [159].
N denotes the number of patients in a particular group.
Certain parameter values are given as mean ± standard deviation.

vestigation, except between frail and non-frail individuals. During walking, the mean cadence, movement vigor, and postural sway were lower by 6 steps/min ($p = 0.038$), 0.04 g ($p = 0.002$), and 0.09 g^2 ($p = 0.021$) in the frail group compared to the non-frail group, respectively. During stair-climbing, the mean cadence was lower by 9 steps/min ($p = 0.037$) in the frail group compared to the non-frail group.

Discussion. Previous research indicates that frail adults often exhibit inferior basic gait values compared to the non-frail group, which is consistent with the results of our work, despite the specifics of the study population. Similarly as in this study, the stride time was found to be 1.0–1.1 s for non-frail and 1.2–1.5 s for frail research subjects in [47, 48]. Meanwhile, cadence was reported to be 117–118 steps/min for non-frail and 85–101 steps/min for frail individuals in [47, 48], with a notable exception in [160] where cadence was equally low in both groups. Movement vigor was also found to be lower among those with frailty, probably due to a slower pace and less intense movements. This finding is in concordance with a previous work reporting considerably more intense movements among non-frail compared to frail adults [160]. In the present study, movement vigor was estimated as a mean amplitude deviation, same as in [142]. However, it can alternatively be expressed as the average of the Euclidean sum of the triaxial accelerations [52], or as a root mean square of acceleration in a particular direction [160] since it largely depends on the signal amplitude.

Due to the plausible interaction between the cognitive and physical frailty [143], it is reasonable to expect an increased gait asymmetry in patients with a worse frailty status. Nevertheless, asymmetry-reflecting measures, i.e., gait asymmetry and the Lissajous index, were the least responsive to inpatient rehabilitation and did not indicate any difference between the non-frail and frail groups. This finding is consistent with the previously reported results where gait asymmetry, gait irregularity, and stride variability did not show a significant difference between the non-frail and pre-frail/frail groups [51]. On the other hand, the opposite results were reported in [160], where stride regularity, step regularity, and step symmetry turned out to be powerful discriminators when estimated from the vertical component of the acceleration signal when using a sensor placed on the trunk [160]. Presumably, dual tasking should be involved to properly explore the effect of the cognitive load on gait asymmetry, as it was shown in elderly patients with Parkinson's disease [50]. However, understanding the relationship between cognitive and physical frailty was outside the scope of the present study.

Parts of Sec. 4.2.3 have been quoted verbatim from the previously published article [17]

4.3. Heart Rate Response

4.3.1. Distribution of unacceptable heart rate series

Table 4.5 sheds light on the distribution of unacceptable HR series for different exercise tests in frail/vulnerable and non-frail patients. Bad fitting of the exponential curve to the recovery phase prevailed in veloergometry and walking, whereas an insufficient HR response was the most common cause of HR series exclusion for stair-climbing and timed up-and-go. No notable difference is observed between the frail/vulnerable and non-frail patients, except for timed up-and-go, which resulted in a two times larger number of excluded tests due to the insufficient HR response in frail/vulnerable compared to non-frail individuals.

4.3.2. Agreement between submaximal testing and veloergometry

Compared to veloergometry, the lowest estimation errors were obtained during walking, which were considerably lower than those during other submaximal tests, see Table 4.6.

Table 4.5. Percentage of unacceptable HR series for different exercise tests in frail/vulnerable (EFS $\geqslant 4$) and non-frail (EFS < 4) patients.

	Frail/Vulnerable	Non-frail	Total
Veloergometry			
No HR response	2.0%	0.0%	1.6%
Bad fitting	5.2%	5.4%	5.2%
Walking			
No HR response	0.7%	0.0%	0.6%
Bad fitting	9.6%	11.1%	9.9%
Stair-climbing			
No HR response	11.9%	14.3%	12.4%
Bad fitting	3.4%	3.6%	3.4%
Timed up-and-go			
No HR response	19.0%	10.7%	17.5%
Bad fitting	11.3%	12.1%	11.4%

Percentages are given for pooled data from before inpatient rehabilitation, after inpatient rehabilitation, and after home-based training.

Table 4.6. Agreement between HR response to veloergometry and each submaximal exercise test.

Submaximal	T_a, s	HRR_{120}, bpm	T_{30}, slope	RES, %
Walking	-66.5 [-97.6, -35.3]	1.6 [0.12, 3.1]	0.04 [0.01, 0.07]	2.2 [-0.4, 4.8]
Stair-climbing	203 [180.7, 225.3]	7.25 [6.0, 8.5]	-0.07 [-0.09, -0.04]	15.9 [13.5, 18.2]
Timed up-and-go	212.9 [185.1, 240.8]	10.9 [9.1, 12.7]	-0.06 [-0.09, -0.03]	18.4 [15.4, 21.4]

The agreement is expressed as mean difference and 95% confidence interval. Results are given for pooled data from before inpatient rehabilitation, after inpatient rehabilitation, and after home-based training.

4.3.3. Relationship between submaximal testing and veloergometry

Fig. 4.2 shows an association between HR response measures estimated during veloergometry and each submaximal exercise test. All submaximal tests show moderate to high correlation for HR recovery measures T_{30} and HRR_{120}, and for HR reserve. On the other hand, none of the submaximal tests induced similar HR acceleration patterns as during veloergometry, which resulted in uncorrelated T_a values.

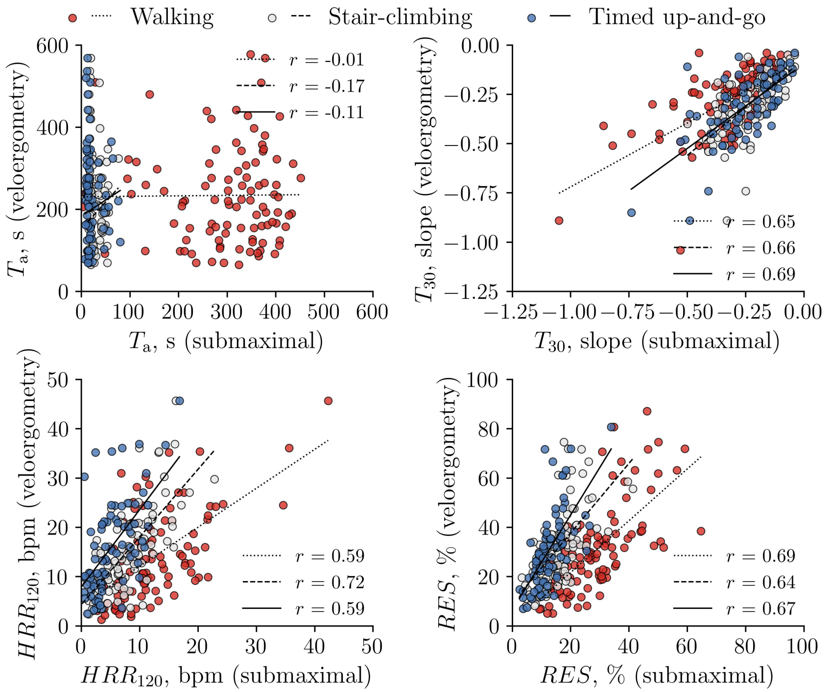


Figure 4.2. Association between HR response measures during veloergometry and submaximal exercise tests. Correlations are given for pooled data from before inpatient rehabilitation, after inpatient rehabilitation, and after home-based training.

Discussion. The selected submaximal tests differ considerably in terms of the induced physical exertion. That is, the patients were asked to ascend 12 stairs during stair-climbing and walk 6 meters during the timed up-and-go test, which was a feasible task for most patients. On the other hand, the ability to perform on the 6-minute walk test largely depends on the patient's functional capacity. As a consequence, the 6-minute walk test resulted in a wide scale of distances, ranging from 150 to 736 meters. The HR response to physical stressors of various intensities is understudied, and therefore it remains an interesting research direction to be explored in the future [63]. For instance, a stronger association between the frailty status and the HR response during normal walking was found compared to rapid walking [63]. This finding may suggest an additional value of submaximal testing for frailty assessment. In addition, submaximal testing showed excellent reproducibility in terms of the HR response at various physical exertions [161].

4.3.4. Relationship of heart rate measures with frailty status

Fig. 4.3 shows associations between the HR response to the veloergometry and baseline HR measures, subdivided into quartiles, and the frailty status. The results indicate an obvious association between the worsening of HR response measures and the deteriorating frailty status, as indicated by an increasing EFS score. The baseline HR measures, namely, resting HR, SampEn, and SDNN, exhibit the same trend until the highest quartile.

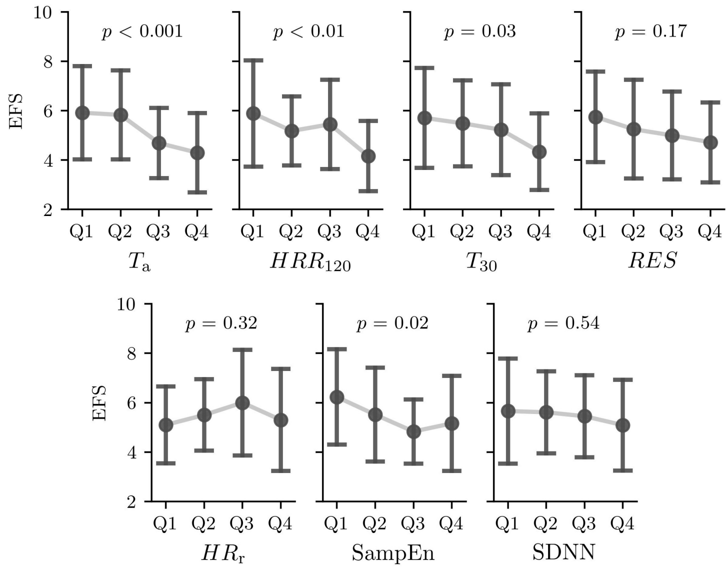


Figure 4.3. Frailty status in quartiles of HR response to veloergometry and baseline HR measures. Results are given as mean $\pm$ standard deviation for pooled data from before inpatient rehabilitation, after inpatient rehabilitation, and after home-based training. p-value refers to the difference in the EFS scores across the corresponding quartiles of HR measures.

4.3.5. Effect of inpatient cardiac rehabilitation

To explore the effect of inpatient rehabilitation on the HR response and baseline HR, the measures were computed before and after rehabilitation for veloergometry and submaximal tests. Veloergometry, walking, stair-climbing, and timed up-and-go tests before and after inpatient rehabilitation were available for 41, 29, 26, and 18 patients, respectively. The HR response measures noticeably changed only for veloergometry. That is, T_a increased from 175$\pm$84 s to 242$\pm$78 s ($p < 0.05$), T_{30} decreased from -0.21$\pm$0.12 to -0.29$\pm$0.14 ($p < 0.05$), HRR_{120} increased from 10.6$\pm$6.2 bpm to 13.9$\pm$7.3 bpm ($p < 0.05$), and RES increased from 23.3$\pm$11.3% to 29.2$\pm$14.6% ($p = 0.05$). No significant change was reflected by walking, stair-climbing, and timed up-and-go.

Discussion. The effect of inpatient cardiac rehabilitation was reflected only by veloergometry. Physical inactivity due to unavoidable bed rest during the early recovery from surgery is the most plausible explanation for the insufficient HR response to submaximal tests [162, 163]. Physical inactivity is associated with autonomic imbalance [162], while cardiac atrophy can already be detected after as little as two weeks of bed rest [164]. The patients spent 17.0±7.4 days recovering from open-heart surgery with minimal or no physical activity, and then were transferred to the rehabilitation hospital. Another important aspect is that patients received beta-blockers altering the HR response through the inhibition of the sympathetic branch of the autonomic nervous system [165]. Despite the inevitability of including those patients who were using HR-affecting medications, the number of medications was balanced in both groups. Furthermore, 14% of the study participants had diabetes mellitus. Cardiac autonomic neuropathy is common in the diabetic population which, in turn, may lead to autonomic imbalance [166].

4.3.6. Effect of the entire exercise training program

Fig. 4.4 shows the effect of the entire exercise training program on the HR response measures in the intervention and control groups. Veloergometry, walking, stair-climbing, and timed up-and-go tests which covered the entire exercise training were available for 30, 25, 22, and 15 patients, respectively. All the HR response measures improved significantly during veloergometry ($p < 0.05$), except for T_a for the control group.

When comparing the submaximal tests with veloergometry, the trends of the measures were best followed during walking, whereas stair-climbing and timed up-and-go seem to be less suitable to capture the change in measures.

No difference is reflected by the change in the values of the HR measures before and after the entire exercise training program between the intervention and the control groups, except for T_a during stair-climbing. The absence of difference corresponds well with similar EFS scores after completing the entire training program in the intervention (4.13±1.45) and the control (4.78±1.66) groups.

Discussion. An increased time to peak HR during walking was observed in frail older adults compared to non-frail individuals [63]. However, the comparison with previous works is complicated since the walking duration, which directly relates to the time of reaching peak HR, differed among the study participants due to the earlier termination of the 6-minute walk test. The changed test duration due to an improved physiological reserve explains why T_a increased during veloergometry but decreased during stair-climbing in the intervention group after the entire exercise training program. That is, the patients were able to continue the veloergometry test 55% longer on average, and thus reach the peak HR later, at end of the training program. Conversely, stair-climbing lasted shorter since the patients were able to climb the stairs faster. Accordingly, the change in the physiological reserve and the ability to sustain physical exertion should be accounted for when considering HR acceleration as a measure for

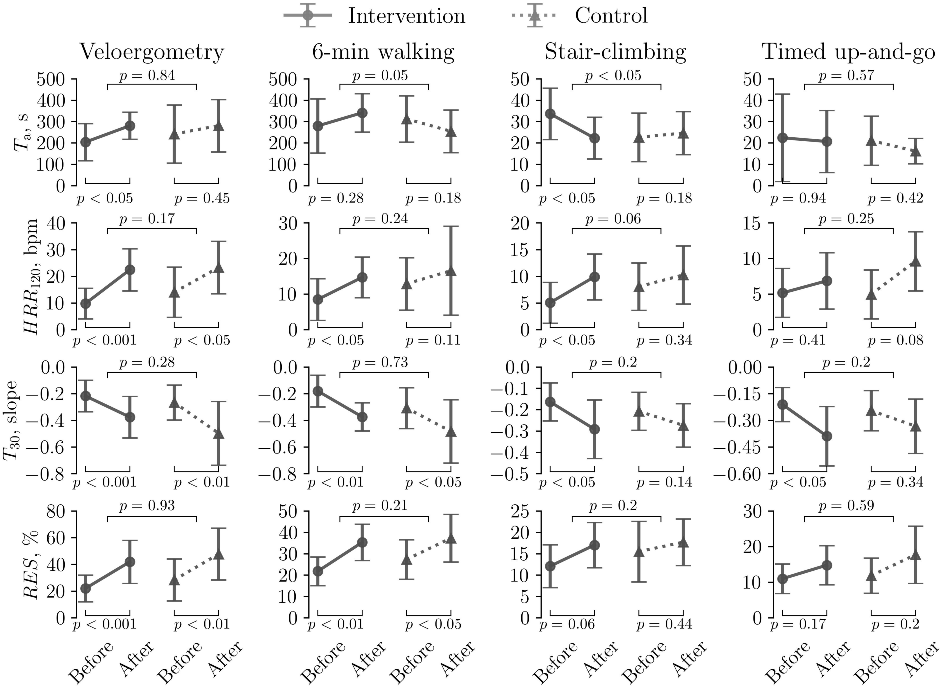


Figure 4.4. Effect of the entire exercise training program on HR response measures in the intervention and control groups. p-value on the top of each subplot refers to the difference in the change of values before and after the entire exercise training program between the intervention and the control groups. p-values on the bottom of each subplot refer to the change in values before and after the entire exercise training program within the intervention and the control groups.

assessing the effectiveness of exercise training programs.

The HR reserve below 80%, at peak exercise, indicates impaired chronotropic response [69]. Despite the fact that the threshold for patients on beta-blockers was reduced to 62% [167], none of the patients managed to reach it at the beginning of the exercise training program. However, 27% of the patients were able to exceed this threshold after completing the program. Even though submaximal testing does not allow to achieve the peak HR, the HR reserve reflected well the tendencies observed while performing veloergometry.

This study showed that resting HR was the least associated with the frailty status. Differently from [60], where the HR complexity, as indicated by the sample entropy, did not differ among frail, pre-frail, and non-frail research subjects, the complexity was associated with the frailty status in our study. When assessing the baseline HR, the effect of HR-altering medication should also be taken into account. A study on the effectiveness of cardiac rehabilitation showed that baseline HR measures, such as variability, were less responsive in those who were taking beta-blockers [168]. Taking this into consideration, it can be assumed that the HR response to exercise may be more beneficial for assessing the autonomic function in patients on beta-blockers than the baseline HR.

Parts of Sec. 4.3 have been quoted verbatim from the previously published article [18]

4.4. Identification of Frailest Physiological Functions

4.4.1. Classification of the components of the Edmonton frail scale

Table 4.7 presents the performance of a gradient boosting decision tree model constructed by using either clinical reference or wearable-based features. The wearable-based model was trained and tested on 121 feature sets, including 73 patients from inpatient rehabilitation, 37 after inpatient rehabilitation, and 11 after home-based training. Meanwhile, the clinical reference model was trained and tested on 157 feature sets, including 82 patients from inpatient rehabilitation, 59 after inpatient rehabilitation, and 16 after home-based training. The model's accuracy, as evaluated by the F_1 score, was 77.8% and 72.7% for the general health status, 71.3% and 65.3% for the functional independence, 72.6% and 76% for nutrition, and 84.7% and 81.0% for the functional performance, when using the clinical reference and estimates from wearable-based biosignals, respectively.

Table 4.7. The performance of the gradient boosting decision trees model using wearable-based features and the clinical reference. Leave-one-out cross-validation is used to evaluate the performance. The performance is evaluated by using F_1 score.

EFS component	Wearable-based measures	Clinical reference measures
General health status	72.7%	77.8%
Functional independence	65.3%	71.3%
Nutrition	76.0%	72.6%
Functional performance	81.0%	84.7%

4.4.2. Interpretation of frailty predictions

The importance of physiological functions in classifying the EFS components is shown in Fig. 4.5. A noticeable observation is that the importance of clinical and wearable-based features differs. For example, wearable-based balance features are found to be more important than those from the clinical reference. Conversely, the gait features from clinical reference are more crucial than the wearable-based features, particularly in identifying the functional performance component.

Figure 4.6 provides an interpretation of classifications for a single patient. In the given example, both wearable-based features and clinical reference contributed

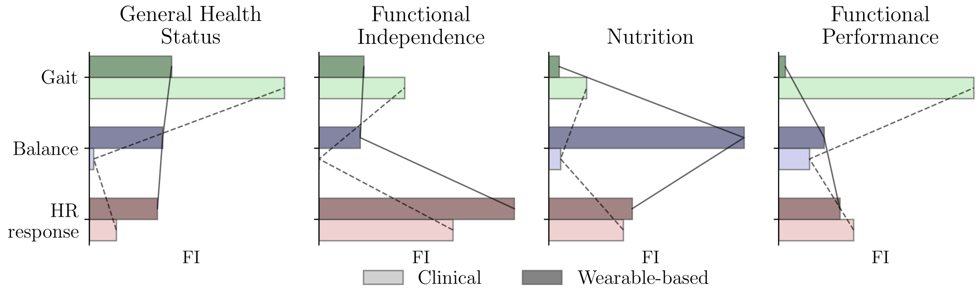


Figure 4.5. Feature importance when classifying EFS components.

similarly in classifying the general health status, the functional independence, and the nutrition components. However, their contributions were opposite when classifying the functional performance component.

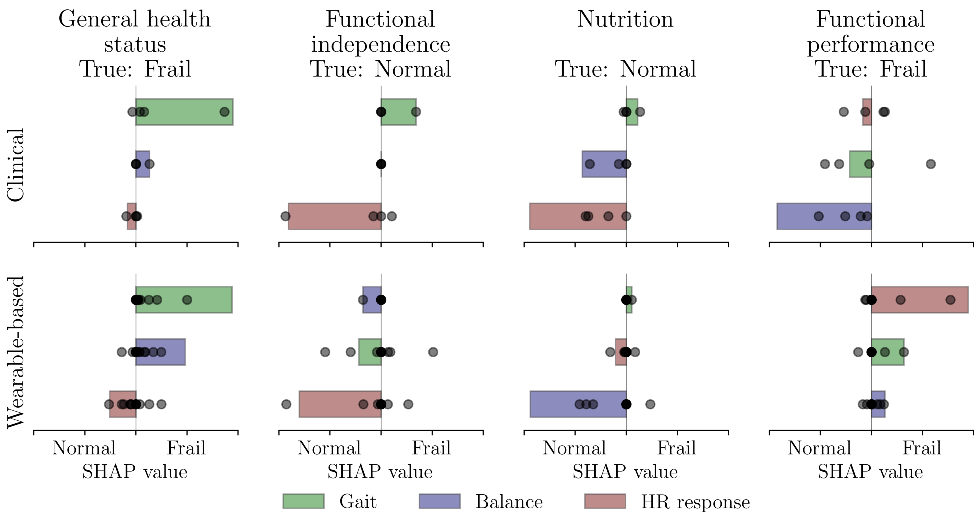


Figure 4.6. Example of an interpretation of classifications for a single patient. SHAP values represent the contribution of a feature towards the outcome of a single prediction.

Figure 4.7 shows the distribution of the SHAP values for the classifications of all patients. Notably, wearable-based features and the clinical reference demonstrated similar contribution tendencies when classifying the general health status, functional independence, and nutrition components. However, distinctly different physiological functions contributed when classifying the functional performance.

If a specific component of the EFS is classified as weak, the physiological function that contributes the most to that classification may be considered as the frailest for the corresponding patient. Table 4.8 presents the percentage of patients in whom the gait, balance, or the heart rate response contributed most to a particular EFS compo-

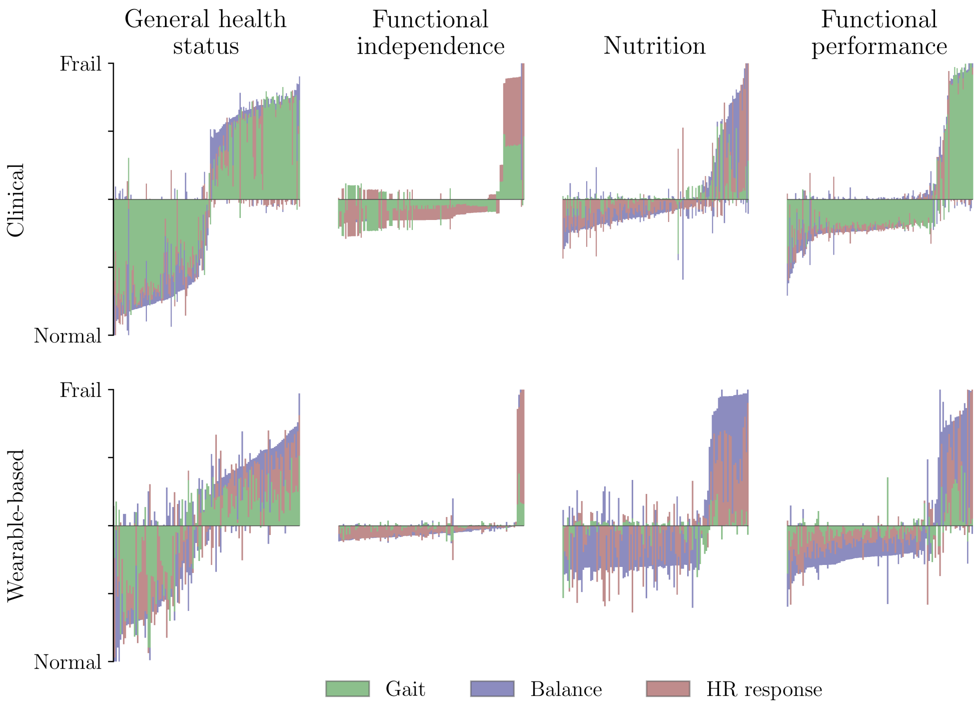


Figure 4.7. Visualization of the distribution of SHAP values for the classifications of all patients. Each vertical bar represents an individual patient.

nent. The results indicate that wearable-based identification of the frailest component aligns with the clinical reference in all cases, except for the functional performance. When determining the general health status, the gait and balance were found to be the predominant contributors to the prediction for 47.9% and 35.5% of patients, respectively. On the other hand, when identifying the functional independence, the heart rate response was the primary contributor for 81.8% of the patients.

Table 4.8. The percentage of patients with physiological functions that contributes the most to classification of a particular EFS component.

Physiological function	General health status	Functional independence	Nutrition	Functional performance
Clinical reference				
Gait	80.9%	33.8%	17.8%	87.9%
Balance	8.9%	0.6%	51.6%	6.4%
Heart rate response	10.2%	65.6%	30.6%	5.7%
Wearable-based				
Gait	47.9%	10.7%	8.3%	7.4%
Balance	35.5%	7.4%	39.7%	36.4%
Heart rate response	16.5%	81.8%	52.1%	56.2%

Discussion. In general, the clinical reference, which involves features obtained from standardized clinical tests and/or specialized equipment, demonstrated better performance in classifying the general health status, functional independence, and functional performance. However, wearable-based features yielded superior performance in classifying the nutrition component. Analysis of the results presented in Figure 4.7 and Table 4.8 suggests that the clinical reference heavily relies on gait-related features, which is expected as the EFS assessment includes such measures as timed up-and-go and the distance walked during the 6-minute walk test.

In contrast, the interpretation of the wearable-based model revealed that all physiological functions contributed to the classification of the EFS component status, thereby suggesting a more comprehensive and multi-dimensional approach to assessing frailty compared to the clinical reference.

4.5. Conclusions of the Chapter

1. The derivative dynamic time warping-based algorithm demonstrated the best overall performance in detecting physical stressors when utilizing the acceleration signal from the vertical axis. Specifically, a sensitivity of 84.2% and a positive predictive value of 82.1% were obtained when assessing walking, while a sensitivity of 81.6% and a positive predictive value of 83.8% were achieved when assessing stair-climbing.
2. The majority of kinematic measures estimated during walking showed an improvement after rehabilitation, along with an improvement in the frailty status. Specifically, the stride time, cadence, postural sway, and movement vigor improved in 71%, 77%, 81%, and 83% of the patients, respectively. However, kinematic measures during stair-climbing showed less improvement compared to walking. Interestingly, home-based exercise training did not result in significant changes in the kinematic measures, which aligns with the minimal deterioration observed in the frailty status.
3. All submaximal tests demonstrated moderate to high correlations (r = 0.59–0.72) with veloergometry for the HR recovery and HR reserve measures. Notably, the effect of inpatient rehabilitation was primarily reflected in the HR response to veloergometry, while the trends of measures over the entire exercise training program were also consistent during stair-climbing and walking.
4. Investigation of an interpretable machine learning model shows that wearable-based performance is comparable to that obtained by using clinical tests. That is, the F_1 score was 77.8% during clinical tests and 72.7% when estimated from wearable-based data for the general health status, 71.3% and 65.3% for functional independence, 72.6% and 76% for nutrition, and 84.7% and 81.0% for the functional performance, respectively.

5. CONCLUSIONS

1. A derivative dynamic time warping-based algorithm has been proposed to detect physical stressors, namely, walking and stair-climbing, in wearable-based biosignals. A sensitivity of 84.2% and a positive predictive value of 82.1% were obtained when assessing walking, while a sensitivity of 81.6% and a positive predictive value of 83.8% were achieved when assessing stair-climbing. The identification of physical stressors in daily activities opens up the possibility to assess the heart rate response to the detected stressors.

2. The feasibility of using a single wearable sensor to track the kinematic properties of frail patients undergoing cardiac rehabilitation after an open-heart surgery has been explored. The stride time, cadence, postural sway, and the movement vigor, derived from wearable-based acceleration signals during walking, improved after rehabilitation, which coincided with an improvement in the frailty status. On the other hand, kinematic measures during stair-climbing showed only a minor improvement, which suggests that walking is a more appropriate physical stressor for assessing the rehabilitation progress. The findings emphasize the value of wearable-based monitoring of the kinematic properties in evaluating the effectiveness of the exercise training programs for frail patients after an open-heart surgery.

3. To comprehensively characterize the heart rate response by relying on the analysis of wearable-based biosignals, measures covering the accelerating phase, the decelerating phase, and the entire heart rate response phase were proposed. The results show a moderate-to-high correlation (ranging from 0.59 to 0.72) between the submaximal tests, such as walking, stair-climbing, and stand up-and-go, and veloergometry for the heart rate recovery and the heart rate reserve measures. Moreover, the findings indicate a clear association between the deteriorating wearable-based heart rate response measures and the worsening frailty status. While the effect of the inpatient rehabilitation was primarily reflected in the heart rate response to veloergometry, the trends observed in the measures during the entire exercise training program were also evident during stair-climbing and walking. Based on these findings, the heart rate response to walking should be considered as a useful measure for assessing the impact of home-based exercise training programs while using wearable devices.

4. A concept of interpretable machine learning has been proposed for identifying clinically informative features which would provide information on the frail physiological functions of an individual patient. The performance of the proposed gradient boosting decision tree model, as evaluated by the F_1 score, was 77.8% and 72.7% for the general health status, 71.3% and 65.3% for functional

independence, 72.6% and 76% for nutrition, and 84.7% and 81.0% for the functional performance when using clinical reference and estimates from wearable-based biosignals, respectively. By targeting the frailest physiological functions, a possibility opens up to tailor exercise programs and improve the functions contributing most of all to frailty for an individual patient.

SANTRAUKA

ĮVADAS

Tyrimo aktualumas

Senatviniam silpnumo sindromui (SSS) būdingas fiziologinio rezervo sumažėjimas ir jautrumas vidiniams (pvz., ligos, operacijos) ir išoriniams (pvz., fizinė veikla) stresoriams [1, 2]. SSS pasireiškia 17 % asmenų, vyresnių nei 60 metų [4], ir tampa vienu iš svarbiausių senėjančios visuomenės iššūkių [3]. SSS susijęs su padidėjusia nepageidaujamų pasekmių, tokių kaip judrumo sutrikimas, negalia, griuvimai ir mirtis, rizika [5]. Laimei, daugėja įrodymų, kad SSS progresavimą galima pristabdyti laiku pritaikius tinkamą intervenciją [6].

Vyresnio amžiaus SSS pacientams po atviros širdies operacijos padidėja pooperacinių komplikacijų rizika, taip pat jiems reikia daugiau laiko išgyti [7]. Atsižvelgiant į sparčiai didėjantį vyresnio amžiaus SSS pacientų, dalyvaujančių širdies reabilitacijos programose, skaičių, tai tampa opia problema, į kurią būtina atkreipti dėmesį [8]. Ši pacientų grupė kenčia nuo sumažėjusios raumenų masės, ištvermės stokos ir susilpnėjusių fiziologinių funkcijų, o tai apsunkina širdies reabilitaciją ir neleidžia taikyti įprastų treniruočių programų [9].

Daugėja įrodymų, kad treniruočių programos gali būti naudingos SSS pacientams, tačiau fizinio aktyvumo užsiėmimų tipas, intensyvumas ir trukmė, taip pat treniravimosi namuose rekomendacijos turi būti kruopščiai pritaikyti kiekvienam asmeniui, kad reabilitacijos tikslai būtų pasiekti nedarant žalos [10,11]. Visgi kai kuriais atvejais treniruočių programos parinkimas ir individualus pritaikymas gali būti problemiškas. Pavyzdžiui, po atviros širdies operacijos įprastai rekomenduojami aerobiniai ir jėgos pratimai, siekiant apsaugoti krūtinkaulį, tačiau SSS gali apriboti įprastinių treniruočių taikymą. Tokiais atvejais, norint padidinti paciento raumenų jėgą, svorį ir mobilumą, gali prireikti asmeniškai pritaikytos programos. Todėl reikia informatyvių ir patogių priemonių treniruočių programų efektyvumui įvertinti, ypač kai programos skirtos pažeidžiamiems pacientams ir numatomos tęsti namų aplinkoje.

Nepaisant to, kad pasiūlyta įvairių indeksų ir klausimynų, apimančių fizinius, fiziologinius, pažintinius ir socialinius gyvenimo aspektus, vis dar nėra visuotinai priimtos standartizuotos SSS vertinimo priemonės [12]. Kadangi klinikiniai įvertinimo metodai netinkami naudoti ne klinikinėje aplinkoje, didėja poreikis naujų žymenų, kurie įgalintų ankstyvą SSS diagnozę ir stebėseną [13]. Tradiciškai moksliniai tyrimai buvo fokusuoti į fizinių žymenų, tokių kaip sulėtėjusi eisena, kurie pirmieji pasireiškia esant SSS, vertinimą [14].

Sisteminė apžvalga ir metaanalizė parodė, kad autonominės nervų sistemos funkciją atspindintys širdies ritmo (ŠR) analize pagrįsti žymenys, tokie kaip širdies ritmo atsakas į krūvį, žemo ir aukšto dažnio sričių spektrinė analizė, ŠR pokyčiai pasikeitus kūno padėčiai, SSS pacientams yra pablogėję [15]. Tai leidžia daryti prielaidą, kad ŠR žymenys gali būti naudingi vertinant širdies gebėjimą normalizuotis paveikus stresoriams ir būtų naudingi vertinant medicininių, fizinių ir mitybos intervencijų poveikį SSS pacientams.

SSS yra kompleksinis sindromas, apimantis įvairias komponentes, tokias kaip fiziologinis rezervas, fiziniai gebėjimai ir pažinimo funkcijos. Dėl šios priežasties svarbu tiksliai nustatyti konkrečias susilpnėjusias komponentes atskiram pacientui ir jas stiprinti taikant individualizuotas treniravimosi programas [16]. Deja, ši tyrimų sritis dar nesulaukė pakankamo dėmesio, todėl trūksta algoritminių sprendimų šiai problemai spręsti.

Mokslinė ir technologinė problema bei darbinė hipotezė

Kol kas SSS įvertinimas apsiriboja tyrimais, atliekamais klinikinėje aplinkoje. Vis dėlto dėvimų įrenginių technologija patobulėjo tiek, kad galima svarstyti galimybę SSS vertinti ir už klinikos ribų. Norint vertinti SSS kasdienėje veikloje, pvz., naudojant dėvimus įrenginius, reikia išspręsti keletą iššūkių, tokių kaip fizinių stresorių atpažinimas ir su SSS siejamų fiziologinių funkcijų įvertinimas.

Mokslinė ir technologinė problema: Kaip informacija, gauta iš dėvimais įrenginiais užregistruotų biosignalų, gali būti panaudota siekiant įvertinti SSS būseną kasdienėje veikloje?

Darbinė hipotezė: Dėvimų įrenginių panaudojimu pagrįsta stebėsena yra tinkama alternatyva siekiant įvertinti SSS būseną už klinikos ribų.

Tyrimo objektas

Šiame darbe vystomi ir tiriami signalų apdorojimo algoritmai, skirti kasdienės veiklos netrukdančiai SSS būsenos ir su SSS siejamų fiziologinių funkcijų stebėsenai.

Tyrimo tikslas

Sukurti, ištirti ir validuoti kasdienės veiklos netrukdančios SSS būsenos stebėsenos algoritmus.

Tyrimo uždavinys yra sukurti, ištirti ir validuoti signalų apdorojimo algoritmus, įgalinančius vertinti SSS būseną naudojant dėvimais įrenginiais užregistruotus biosignalus. Konkrečiai disertacijoje tiriami algoritmai skirti:

1. atpažinti fizinius stresorius;
2. įvertinti kinematines savybes;
3. įvertinti širdies ritmo atsaką į fizinius stresorius;
4. identifikuoti nusilpusias fiziologines funkcijas individualiam pacientui.

Tyrimo tikslas – sukurti, ištirti ir patvirtinti signalų apdorojimo algoritmus, leidžiančius įvertinti individo silpnumo būseną naudojant nešiojamus biosignalus. Konkrečiai darbe siūlomi ir tiriami fizinių stresorių aptikimo algoritmai; kinematinių savybių įvertinimas; širdies ritmo reakcijos į fizinius stresorius įvertinimas; silpniausių fiziologinių funkcijų nustatymas.

Mokslinis naujumas

Didėjant SSS pacientų, kuriems atliekamos operacijos, skaičiui, reikia tinkamų sprendimų, kurie padėtų geriau suprasti ir įvertinti treniravimo plano efektyvumą [9]. Atsižvelgiant į patogių stebėsenos technologijų poreikį, disertacijoje pasiūlytas ir ištirtas kasdienės veiklos nevaržantis SSS įvertinimo būdas.

Dauguma ankstesnių tyrimų buvo skirti SSS ir ankstyvajai SSS stadijai atpažinti, tačiau galimybė stebėti subtilius SSS pokyčius treniruočių metu dar nebuvo išsamiai nagrinėta. Disertacijos tyrimai, kuriuose nagrinėjimas kinematinių ir ŠR atsako parametrų tinkamumas SSS trajektorijai sekti treniruotėmis pagrįstos reabilitacijos metu, užpildo šią tyrimų spragą. Pasiūlytas būdas visapusiškai ištirtas su pacientais, kurie vykdė padidinto intensyvumo reabilitaciją klinikoje bei mažesnio intensyvumo treniravimosi programą namuose. Pasiūlytas būdas gali būti taikomas vertinant SSS būklę treniruočių namuose metu ir atpažįstant ankstyvuosius SSS požymius.

Sukurti algoritmai leido dėvimais įrenginiais užregistruotuose biosignaluose įvertinti kinematines SSS pacientų savybes. Rezultatai parodė, kad dauguma kinematinių parametrų pagerėjo daugumai pacientų, o tai atitiko SSS gerėjimo tendenciją. Vykdant treniruočių programą namuose, nepastebėta ryškesnių kinematinių parametrų pokyčių.

Sukurtais algoritmais vertinant ŠR atsaką į fizinius stresorius pastebėta, kad daugeliui SSS pacientų ŠR atsakas pagerėjo. Pagerėjimas didžiausias intervencijos grupėje, kuriai buvo paskirta treniruočių programa namuose, kas leidžia daryti prielaidą, kad treniravimasis namuose yra tinkama intervencija fiziologiniam rezervui pagerinti. Vertinant galimybes taikyti algoritmus kasdienėje veikloje, nustatyta, kad spartus ėjimas ir lipimas laiptais tinkamiausi sukelti ŠR atsaką, kurio pakaktų sekti parametrų tendencijas, stebimas naudojant klinikinį standartą – veloergometriją.

Pasiūlytas interpretuojamas mašininiu mokymusi pagrįstas algoritmas, skirtas nusilpusioms konkretaus paciento fiziologinėms funkcijoms identifikuoti. Pasiūlytas būdas leidžia susieti SSS stadiją su specifiniais SSS bruožais, o tai gali suteikti papildomos informacijos gydytojams kuriant individualizuotas treniruočių programas. Pasiūlytas būdas turi pontencialo įgalinti geriau suprasti kiekvieno paciento SSS būklę ir sudarant sąlygas efektyviau taikyti esamas reabilitacijos priemones.

Praktinė reikšmė

1. Siūlomas SSS būsenos vertinimo būdas gali būti taikomas šiais atvejais:
   (a) SSS būklei vertinti treniravimosi programos namuose metu.
   (b) Kasdienės veiklos nevaržančiai SSS pacientų stebėsenai ir ankstyvai SSS stadijai nustatyti.
   (c) Pagalbinė priemonė gydytojams kuriant individualizuotas treniravimosi programas.
   (d) Pagalba gydytojams siekiant geriau suprasti labiausiai nusilpusias konkretaus paciento fiziologines funkcijas.

2. Šiame darbe pasiūlyti būdas ir algoritmai sukurti įgyvendinant projektus „Kasdienės veiklos nevaržančios autonominės nervų sistemos funkcijos stebėsenos technologijos senatvinį silpnumo sindromą turintiems pacientams – FrailHeart“ (P-MIP-20-95), 2020–2022 ir „Interpretuojamas mašininio mokymo algoritmas senatvinio silpnumo sindromui vertinti – intFrail“ (Nr. PP2022/58/2), 2022.

Tyrimo aprobavimas

Daktaro disertacija remiasi dviem pagrindiniais straipsniais, publikuotais tarptautiniuose moksliniuose žurnaluose, turinčiuose cituojamumo rodiklį „Clarivate Analytics Web of Science“ duomenų bazėje. Taip pat publikuoti du susiję su tyrimų tema straipsniai. Pagrindiniai rezultatai pristatyti konferencijose „BIOSIGNALS 2021: 14^{th} International Conference on Bio-inspired Systems and Signal Processing“ ir „19^{th} Nordic-Baltic Conference on Biomedical Engineering and Medical Physics“. Tyrimas, pristatytas „BIOSIGNALS 2021“ konferencijoje, įvertintas geriausio studentų straipsnio apdovanojimu.

Ginti teikiami teiginiai

1. Lipimo laiptais ir ėjimo veiklos tinkamos alternatyvos įprastiniams, klinikose taikomiems fizinio aktyvumo testams, o fizinio aktyvumo tipą galima nustatyti kasdienės veiklos metu, analizuojant pagreičio signalus, gautus naudojant dėvimus įrenginius.
2. SSS tendencijų stebėsena treniruočių metu, naudojant kinematinius parametrus, gautus iš vieno dėvimo jutiklio, gali būti alternatyva įprastiems klinikiniams fizinio aktyvumo testams.
3. ŠR atsakas į fizinius stresorius gali būti naudojamas vertinant treniruočių programų efektyvumą SSS pacientams.
4. Identifikuoti susilpnėjusias fiziologines funkcijas galima naudojant interpretuojamą mašininio mokymosi algoritmą.

Bendradarbiavimas

Kinematinių charakteristikų vertinimo tyrimai atlikti bendradarbiaujant su dr. Monika Butkuviene (Biomedicininės inžinerijos institutas, KTU). Tyrimai vertinant ŠR atsaką atlikti bendradarbiaujant su prof. Raquel Bailon-Luesma (Biomedicininių signalų interpretavimo ir modeliavimo grupė, Saragosos universitetas, Ispanija). Tyrimų duomenų bazę surinko Lietuvos sveikatos mokslų universiteto klinikų ir Kauno klinikų Kulautuvos reabilitacijos ligoninės sveikatos priežiūros specialistai (Eglė Tamulevičiūtė-Prascienė, Aurelija Beigienė, Vitalija Barasaitė), vadovaujant prof. Raimondui Kubiliui.

1. APŽVALGA

SSS yra vyresniems žmonėms įprastai pastebima būklė, kuriai pasireiškus būdingas fiziologinio rezervo sumažėjimas ir padidėjęs jautrumas įvairiems stresoriams [19]. SSS pasireiškia įvairiose organų sistemose ir sukelia neigiamų sveikatos pasekmių, įskaitant mobilumo sumažėjimą, negalią, hospitalizavimą ir mirtį [1]. Nors SSS dažnai lėtinis ir progresuojantis – tai ne visada reiškia negrįžtamą progresavimą iki visiško nusilpimo. Daugėja įrodymų, kad tinkamos intervencijos, tokios kaip treniravimosi programos, gali pristabdyti progresavimą arba net pagerinti SSS būklę [6, 20, 21].

Didėjantis SSS pacientų, įsitraukiančių į širdies reabilitacijos programas, skaičius kelia didelį susirūpinimą, nes SSS pacientams gresia didesnė chirurginių intervencijų, ilgesnio sveikimo, pooperacinių komplikacijų ir mirštamumo ligoninėje rizika [8]. SSS pacientams po atviros širdies operacijos svarbus tinkamo treniruočių programos tipo ir intensyvumo parinkimas, nes būtinybė saugoti krūtinkaulį dažnai apriboja įprastų treniravimosi programų taikymo galimybes [9]. Organizmo reakcija į programas gali būti skirtinga, todėl, siekiant reguliariai įvertinti treniruočių programos efektyvumą, reikia patogių ir informatyvių metodų, ypač kai treniruotės tęsiamos namuose. Pasiūlyta įvairių SSS būklės įvertinimo būdų [12], tačiau vis dar nėra universalaus ir pripažinto standarto. Taip yra dėl išskirtinai daugiakomponentinio SSS pobūdžio, apimančio fizinius, psichologinius, pažintinius ir socialinius veiksnius. Negana to, esami klinikiniai SSS įvertinimo būdai dažnai reikalauja specialistų priežiūros, o tai riboja jų pritaikymą už klinikos ribų.

Treniruočių programos, apimančios jėgos, aerobikos, pusiausvyros ir koordinacijos pratimus, turi potencialo pagerinti SSS pacientų eiseną, pusiausvyrą ir fizinį pajėgumą, nors optimalios šių treniruočių charakteristikos (pvz., tipas, dažnis ir trukmė) lieka neaiškios [3,10,27,28]. Nustatyti optimalias treniruočių charakteristikas sudėtinga dėl nestandartizuotų reabilitacijos klinikų programų rengimo skirtumų, o tai apsunkina įvairių taikomų treniruočių programų palyginimą. Siekiant įveikti šiuos iššūkius, svarbu sutelkti pastangas kuriant visapusius ir praktiškus SSS būklės vertinimo būdus, kurie galėtų būti taikomi ir už klinikos ribų.

Friedo silpnumo fenotipas – populiarus klinikinis SSS būklės įvertinimo būdas, ypač dažnai naudojamas atliekant tyrimus, kuriuose taikomi kinematiniai mobilumą įvertinantys parametrai [13]. Friedo silpnumo fenotipas remiasi fizinių komponenčių, tokių kaip svorio kritimas, nuovargis, sulėtėjęs eisenos tempas ir mažas fizinis aktyvumas, vertinimu, todėl laikomas vienu iš objektyviausių SSS būklės vertinimo būdų. Edmontono silpnumo skalė (EFS) papildomai atsižvelgia į socialinius, pažintinius ir mitybos aspektus [29]. EFS įvertina funkcinį pajėgumą, remiantis „stokis ir eik“ testu, įvertinančiu eisenos tempą ir pusiausvyrą. Nepaisant to, kad EFS gana subjektyvus, šis būdas įvairiuose tyrimuose išsiskyrė patikimumu ir atkartojamumu [12, 29, 30].

Ilgalaikiai SSS progreso tyrimai atskleidė, kad nuovargis, silpnumas, mažas fizinis aktyvumas ir lėtas eisenos tempas yra vieni pirmųjų SSS požymių [21]. Todėl nenuostabu, kad fizinių funkcijų, kurios atsispindi fizinio aktyvumo, eisenos ir pusiausvyros parametruose, sutrikimo vertinimas, yra ypač vertingas atpažįstant SSS būsenas [13, 43]. Paprastai kinematiniai parametrai įvertinami atliekant klinikinius testus, kuriems būtina medicinos darbuotojų priežiūra [39], tačiau stebėsenai už klinikos ribų įprastos kasdienės veiklos, tokios kaip ėjimas ar lipimas laiptais, turi potencialo geriau atspindėti tikrąją tiriamojo fizinę būklę [39].

Širdies ir kraujagyslių funkciją reguliuoja autonominė nervų sistema, todėl keliama hipotezė, kad širdies autonominis disbalansas prisideda prie SSS pablogėjimo [14, 26, 59, 60], o tai savo ruožtu gali sumažinti gebėjimą išlaikyti homeostazę veikiant fiziniams stresoriams [14, 61]. Autonominė nervų sistema kontroliuoja ŠR, todėl matomi ŠR pakitimai – padidėjęs ŠR ramybės būsenoje, sumažėjęs ŠR kompleksiškumas ir variabilumas, lėtesnė ir silpnesnė ŠR reakcija į fizinį krūvį ir susilpnėjęs ŠR normalizavimasis po fizinio krūvio [14, 62].

ŠR atsakas į ėjimą jau buvo sietas su SSS būsena [63]. Ankstesni tyrimai parodė, kad po ėjimo ŠR atsakas vyresnio amžiaus SSS pacientams yra lėtesnis ir silpnesnis, palyginti su sveikais asmenimis, o tai rodo, kad ŠR parametrai gali būti naudingi vertinant SSS būklę. Tyrime sutelktas dėmesys tik į normalų ir greitą ėjimą, todėl lieka neaiškus kitų fizinių stresorių poveikis ŠR atsakui. Be to, turimi duomenys apėmė tik trumpą laikotarpį — 5 sekundes prieš ir 10 sekundžių po ėjimo, o tai riboja ramybės ŠR charakterizavimo galimybes. Atsižvelgiant į šiuos trūkumus, tyrimo autoriai išreiškė didelį susidomėjimą ištirti ramybės ŠR kompleksiškumą ir ŠR normalizavimosi parametrus [63].

2. DUOMENŲ BAZĖ

SSS pacientų stebėsenos algoritmams vystyti ir tirti užregistruota biosignalų ir atraminių klinikinių duomenų bazė. Elektrokardiogramos ir trijų ašių pagreičio signalai užregistruoti atitinkamai 130 Hz ir 200 Hz diskretizavimo dažniu, panaudojant tekstilinį krūtinės diržą su nešiojamu jutikliu (Polar H10; Polar Electro OY, Kempele, Suomija). Kaupiant duomenų bazę, įvertinti 337 pacientai, atvykę į Kulautuvos reabilitacijos ligoninę po širdies operacijos. Iš jų 100 atitiko numatytus įtraukimo kriterijus, t.y. vyresnis nei 65 m. amžius, nustatytas SSS, pakankamas fizinis pajėgumas bei atmetimo kriterijų nebuvimas. SSS įvertintas EFS įverčiu, kuris gali būti nuo 0 iki 17. Atsižvelgiant į balų skaičių, išskiriamos trys SSS stadijos: $\leqslant$3 — nėra SSS, 4–5 — pažeidžiami, $\geqslant$6 — SSS.

2.1 lentelė. Pacientų demografiniai ir klinikiniai duomenys intervencinėje ir kontrolinėje grupėse.

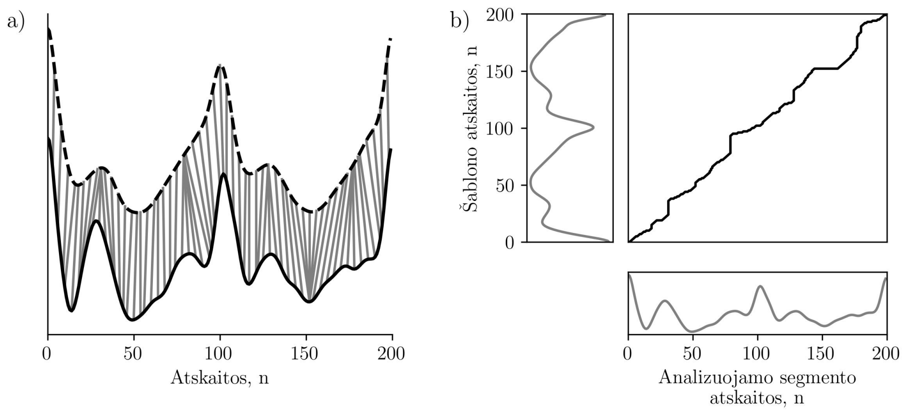
Kintamasis	Intervencinė	Kontrolinė
Moterys	25	13
Vyrai	25	37
Amžius, metai	73,2 ± 4,8	73,4 ± 5,3
Ūgis, cm	165,9 ± 8,6	169,4 ± 8,6
Svoris, kg	74,9 ± 12,8	78,7 ± 13,2
Kūno masės indeksas, kg/m2	27,3 ± 4,8	27,4 ± 3,9
Laikas po operacijos, dienos	16,6 ± 7,3	17,6 ± 7,5
Medikamentai		
Angiotenziną konvertuojantis fermentas	37	40
β adrenoblokatoriai	49	50
Kalcio kanalų blokatoriai	2	1
Širdies nepakankamumo klasė		
NYHA I	2	3
NYHA II	40	34
NYHA III	8	13
Fizinis pajėgumas		
Maksimalus pasiektas krūvis, W	49,5 ± 15,8	51,0 ± 15,5
Veloergometrijos trukmė, s	161,8 ± 97,8	154,4 ± 95,2
6 min ėjimo atstumas, m	289 ± 86,1	291 ± 79,6
„Stokis ir eik“ trukmė, s	8,9 ± 2,4	8,5 ± 1,7
Edmontono silpnumo skalės įvertis	6,2 ± 1,6	6,0 ± 1,6

Prieš pradedant reabilitaciją, pacientai atsitiktiniu būdu suskirstyti į intervencinę ir kontrolinę grupes. Grupės gerai suderintos, išskyrus tai, kad kontrolinėje grupėje buvo kur kas daugiau vyrų (2.1 lentelė). Intervencinės grupės pacientams atlikti kontroliniai telefono skambučiai kas dvi savaites teiraujantis, ar laikomasi sudarytos fizinio treniravimosi namuose programos.

3. METODAI

3.1 Fizinių stresorių atpažinimo algoritmas

Sukurtas dinaminiu laiko skalės iškreipimu pagrįstas algoritmas fiziniams stresoriams atpažinti. Algoritmas priima sprendimą apie fizinio stresoriaus tipą (pvz., ėjimas ar lipimas laiptais), įvertindamas dviejų signalo segmentų panašumą nepriklausomai nuo laiko vėlinimo bei signalo formos ištempimo ar suspaudimo laiko ašyje (3.1 pav.). Signalo sutapimas įvertinamas apskaičiuojant atstumų sumą tarp šablono ir analizuojamo signalo segmento atskaitų. Šablono parinkimas ėjimo ir lipimo laiptais stresoriams turi esminę svarbą, nes šablonas turi būti pakankamai detalus, kad skirtųsi nuo kitų judesių, bet ne per daug specifiškas. Lyginant ėjimo ir lipimo laiptais šablonus su analizuojamu segmentu bei nustačius optimalų sutapimą, segmentas priskiriamas tai veiklai, kuriai paklaida gaunama mažesnė.



3.1 pav. Dinaminiu laiko skalės iškreipimu pagrįsto algoritmo, skirto atpažinti fizinius stresorius, veikimo principas: a) analizuojamo segmento (ištisinė linija) sulyginimas su šablonu (brūkšninė linija) ir b) optimalus signalų sutapdinimas

3.2 Kinematiniai parametrai

Eisena ir balansas įvertinami analizuojant trijų ašių pagreičius: priekinį-šoninį (Acc_{AP}), vertikalų (Acc_V) ir vidurio (Acc_{ML}). Pagreičio signalą sudaro dinaminė komponentė, atsirandanti dėl greičio pokyčių judėjimo metu, bei statinė gravitacijos komponentė. Gravitacijos įtaka eliminuota trendo pašalinimo būdu. Žingsnio trukmė, ėjimo tempas ir eisenos asimetrija įvertinti radus žingsnio ilgį Acc_V signale, nufiltruotame 3 eilės žemųjų dažnių Butterworth filtru, kurio pjūvio dažnis 2,5 Hz. Judėjimo intensyvumas įvertintas neapdorotame pagreičių signale, prieš tai pašalinus gravitacijos komponentę. Vertinant Lisažu indeksą ir pusiausvyros svyravimus, lėti kūno judesiai, pvz., dėl kvėpavimo, nuslopinti 3 eilės Butterworth aukštųjų dažnių filtru, kurio pjūvio dažnis 0,3 Hz. Triukšmas pašalintas naudojant 3 eilės Savitzky ir Golay glotninamąjį filtrą, kurio lango ilgis – 41.

Tyrimai rodo, kad **žingsnio trukmė** ilgėja esant sunkesnei SSS stadijai [43, 51]. Žingsnio trukmė atspindi eisenos ciklo trukmę ir apibrėžiama kaip laikas, praėjęs tarp dviejų iš eilės tos pačios kojos žingsnių pirmųjų kontaktų su žeme. Nufiltruotame Acc_V signale pikai atitinka dešine arba kaire koja atliekamą žingsnį. Laiko intervalas tarp gretimų pikų atitinka vieno žingsnio, atliekamo dešine arba kaire koja, trukmę, o intervalas tarp kas antrojo piko atitinka bendrą žingsnio ilgį, kurį sudaro pakaitomis einantys du žingsniai.

SSS asmenims dažnai būdingas sulėtėjęs **eisenos tempas**, todėl šis įvertis gali būti taikomas nustatant pirmines SSS stadijas [49, 141]. Eisenos tempas išreiškiamas kaip žingsnių skaičius per minutę analizės laiko intervale T.

Judėjimo intensyvumas tiesiogiai daro įtaką pagreičio signalo amplitudei, todėl ypač gerai tinka fizinio aktyvumo intensyvumui kategorizuoti [52, 142]. Kadangi SSS pacientai dažnai juda lėčiau, sumažėja judėjimo intensyvumas, kuris šiame tyrime įvertintas vidutiniu amplitudės nuokrypiu:

$$Intensyvumas = \frac{1}{n} \sum_{i=1}^{n} \left| Acc(i) - \overline{Acc} \right|, \tag{3.1}$$

čia $Acc(i)$ yra trijų ašių pagreičio signalo atskaitų euklidinis atstumas, $\overline{Acc}$ – vidutinė Acc reikšmė ir n – atskaitų skaičius analizės laiko intervale T.

Sveikiems asmenims nereikia kognityvinių pastangų siekiant išlaikyti pusiausvyrą, tačiau kognityvinių pastangų reikalauja kai kurios patologinės būsenos [50]. SSS neigiamai veikia kognityvines funkcijas [143], todėl yra pagrindo manyti, kad SSS pacientų eisena gali būti labiau asimetriška dėl negebėjimo susitvarkyti su papildoma kognityvine apkrova. Eisenos asimetrija, apibūdinanti kairiojo ir dešiniojo žingsnių koordinaciją, randama pagal formulę:

$$Asimetrija = \frac{1}{k} \sum_{i=1}^{k} \frac{|t_l(i) - t_r(i)|}{t_l(i) + t_r(i)} \times 100, \tag{3.2}$$

čia k yra žingsnių skaičius analizės laiko intervale T, $t_l(i)$ ir $t_r(i)$ atitinkamai kairiojo ir dešiniojo žingsnių trukmės. Artima nuliui vertė rodo simetrišką eiseną, o didėjančios vertės – didėjančią asimetriją.

Lisažu indeksas įvertina judesių simetriją pagreičio šoninėje plokštumoje [56]. Lisažu indeksas apskaičiuojamas randant skirtumą tarp stačiakampių, gaubiančių spageti diagramą, gautą pavaizduojant pagreičio signalą vertikalioje plokštumoje su pagreičio signalu šoninėje plokštumoje:

$$Lisažu\ indeksas = 2\frac{|Plotas_t - Plotas_n|}{Plotas_t + Plotas_n} \times 100, \tag{3.3}$$

čia $Plotas_t$ ir $Plotas_n$ yra atitinkamai teigiamų ir neigiamų spageti diagramos pusių stačiakampių plotai. Nuliui artima Lisažu indekso vertė rodo puikią judesių simetriją ir didėja didėjant asimetrijai.

Pusiausvyros svyravimai įvertinami remiantis spageti diagrama, gauta vaizduojant pagreičio signalą priekinėje-užpakalinėje plokštumoje su pagreičio signalu šoninėje plokštumoje [46]. Tokia spageti diagrama apgaubiama randant mažiausią išgaubtą daugiakampį, apimantį visus duomenų taškus. Bendras apgaubtas plotas apibūdina pusiausvyros svyravimus.

3.3 Širdies ritmo atsako parametrai

Prasidėjus fiziniam krūviui, ŠR pradeda didėti dėl parasimpatinės nervų sistemos slopinimo ir simpatinės nervų sistemos aktyvavimosi. Pasibaigus krūviui, ŠR sumažėja iki pradinio lygio dėl parasimpatinės nervų sistemos reaktyvacijos ir simpatinės nervų sistemos slopimo. Norint visapusiškai apibūdinti ŠR atsaką į fizinį stresorių, pasirinkti ŠR parametrai, apimantys ŠR augimo ir lėtėjimo fazes bei bendrą ŠR atsako intervalą.

ŠR augimo fazė charakterizuojama laiko intervalu T_a, kuriame ŠR greitėja, kol pasiekia didžiausią ŠR fizinio stresoriaus metu (HR_p). Pastebėta, kad vyresnio amžiaus žmonių, kuriems nustatytas SSS, laikas iki didžiausio ŠR ilgesnis, palyginti su nesergančiais SSS [63].

ŠR įprastai normalizuojasi eksponentiškai, sparčiai mažėja pirmąją minutę pasibaigus fizinei apkrovai, po to mažėja lėčiau, kol pasiekiamas pradinis ŠR. Greitajai normalizavomosi fazei charakterizuoti skaičiuojama laiko konstanta (T_{30}), kuri randama pritaikant tiesę prie logaritmuotos ŠR sekos 30 s laiko lange nuo normalizavomosi pradžios taško. Lėtajai normalizavomosi fazei charakterizuoti skaičiuojamas ŠR sumažėjimas 120 s nuo normalizavomosi pradžios (HRR_{120}). Lėtesnis ŠR normalizavimasis gali įspėti apie autonominę disfunkciją bei padidėjusią širdies ir kraujagyslių ligų riziką.

Bendras ŠR atsakas įvertintas ŠR rezervu, kuris apima tiek ramybės, tiek fizinio aktyvumo fazes ir nepriklauso nuo amžiaus, ramybės ŠR bei fizinio pasirengimo [148]. ŠR rezervas randamas pagal formulę:

$$RES = \frac{HR_\mathrm{p} - HR_\mathrm{r}}{HR_\mathrm{a} - HR_\mathrm{r}} \times 100, \tag{3.4}$$

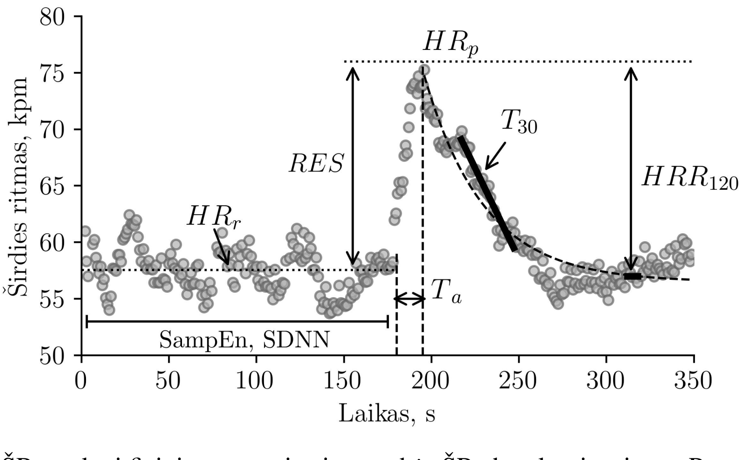
čia HR_r yra ramybės ŠR, apskaičiuotas ramybės fazėje prieš fizinį krūvį, ir HR_a yra maksimalus pasiekiamas individualus ŠR (220 – amžius). Sveikų žmonių RES fizinio krūvio metu yra apie 100 %, o žemas RES gali įspėti apie sutrikusį chronotropinį atsaką. Slenkstinis $RES < 80$ % gali įspėti apie sutrikusį chronotropinį atsaką, o pacientams, vartojantiems beta blokatorius, slenkstinė RES vertė < 62 % [74].

Padidėjęs ramybės ŠR, sumažėjęs ŠR kompleksiškumas ir variabilumas siejamas su autonominiu disbalansu, kuris pasireiškia padidėjusiu simpatiniu ir (arba) sumažėjusiu parasimpatiniu aktyvumu [62]. Padidėjęs ramybės ŠR laikomas mirtingumo nuo širdies ir kraujagyslių ligų rizikos veiksniu [149]. Taip pat pastebėta, kad ramybės ŠR didesnis SSS asmenims [136].

Ramybės ŠR kompleksiškumas įvertintas imties entropijos (SampEn) parametru [150]. Atsižvelgiant į ŠR sekos profilio ilgį m ir panašumo slenkstį r, kurį viršijus ŠR profiliai laikomi panašiais, SampEn įvertina tikimybę, kad panašūs m ilgio ŠR profiliai išliks panašūs padidinus profilio ilgį iki $m + 1$. Reguliaraus ŠR metu SampEn artėja į 0 ir įgauna didesnes reikšmes didėjant ritmo kompleksiškumui. Šiame tyrime konstanta r parinkta 0,15 s, o m – 2 [60]. Sumažėjęs ŠR kompleksiškumas gali įspėti apie autonominę disfunkciją SSS pacientams.

Ultratrumpalaikiam ŠR variabilumui vertinti [151] apskaičiuotas RR intervalų standartinis nuokrypis (SDNN). Sumažėjęs variabilumas gali įspėti apie asmenų, kuriems pasireiškia SSS, parasimpatinės veiklos nuslopimą [60].

Skaičiuojami ŠR atsako į fizinius stresorius ir ramybės ŠR parametrai pateikti 3.2 pav.



3.2 pav. ŠR atsako į fizinius stresorius ir ramybės ŠR charakterizavimas. Pastaba: RES normalizuotas [(200 – amžius) – R_{r}]. Fizinio krūvio pradžia ir pabaiga atitinkamai 180 s ir 195 s

3.4 Nusilpusių fiziologinių funkcijų identifikavimo algoritmas

Sukurtas interpretuojamu mašininiu mokymusi pagrįstas nusilpusių fiziologinių funkcijų identifikavimo algoritmas. Požymiai mašininio mokymosi algoritmui parinkti atsižvelgiant į fiziologines funkcijas, kurias jie charakterizuoja. Tyrimui atrinkti du požymių rinkiniai: išskirti iš dėvimais įrenginiais užregistruotų signalų ir atraminiai klinikiniai.

Požymiai, išskirti iš dėvimais įrenginiais užregistruotų signalų, sugrupuoti į fiziologines funkcijas, t. y. charakterizuojantys eiseną, balansą ir ŠR atsaką. Eiseną charakterizuojantys požymiai – žingsnių skaičius, eisenos tempas, ėjimo nereguliarumas ir judėjimo intensyvumas. Pusiausvyrą charakterizuojantys požymiai – eisenos asimetrija, pusiausvyros svyravimai, pusiausvyros svyravimo nereguliarumas ir Lisažu indeksas. ŠR atsaką charakterizuojantys požymiai – HRR_{60}, HRR_{120}, T_{30}, RES, HR_{max} ir T_a. Visi požymiai įvertinti ėjimo ir lipimo laiptais testų metu.

Eiseną charakterizuojantys klinikiniai požymiai – „stokis ir eik“ testo įvertis, nueitas atstumas 6-min ėjimo testo metu ir eisenos greitis. Pusiausvyros požymiai – žingsnio plotis, eisenos asimetrija, dvigubos atramos dalis eisenos metu ir pusiausvyros centro kitimas. Pastarieji požymiai gauti naudojant klinikinę eisenos ir balanso įvertinimo įrangą Zebris FDM-T. ŠR atsako požymiai – HRR_{60}, HRR_{120}, RES, T_{30}, HR_{max} ir T_a, įvertinti veloergometrijos testo metu.

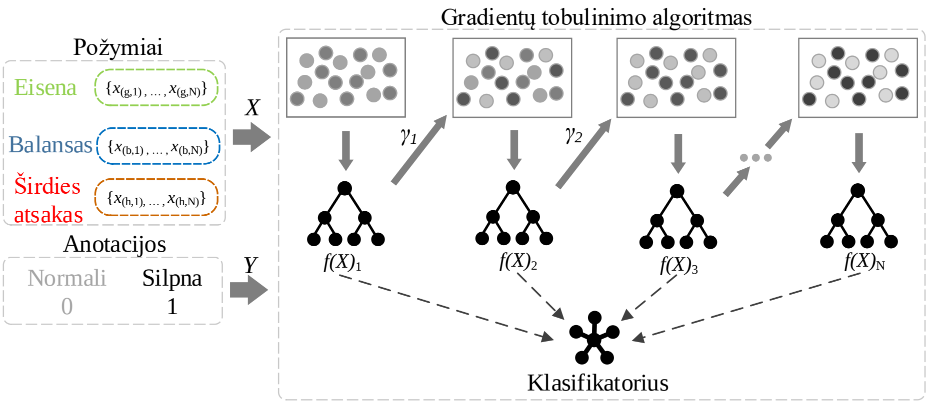
Taip pat abiem atvejais įtraukti asmens charakteristikas apibūdinantys požymiai – amžius, kūno masės indeksas ir laikas po širdies operacijos.

Duomenų bazę sudaro sąlyginai daug požymių, bet mažai duomenų, todėl nusilpusioms fiziologinėms funkcijoms identifikuoti pasirinktas sprendimų medžio modelis. Sprendimų medžio modelis randa optimalią slenkstinę vertę kiekvienam iš požymių vis mažinant klasifikavimo paklaidą. Modelis vystomas rekursyviai – padalijant duomenis į vis mažesnes grupes, atitinkančias tam tikrą kategoriją. Padalijimas atliekamas taip, kad gautos grupės kuo tiksliau atitiktų joms priskirtas kategorijas.

Optimali slenkstinė vertė randama apskaičiuojant informacijos išlošio įvertį, kuris įvertina kiekvienos iš grupių entropijos sumažėjimą po padalijimo. Padalijimo procesas tęsiasi tol, kol pasiekiami pabaigos kriterijai: maksimalus modelio gylis arba minimalus imties skaičius grupėje. Siekiant pagerinti sprendimų medžių modelio tikslumą, pritaikytas jungtinis gradiento tobulinimo algoritmas. Pasiūlyto algoritmo struktūra pateikta 3.3 pav. [153].

EFS įvertina skirtingus sveikatos būklės aspektus [154], todėl daroma prielaida, kad skirtingi požymiai turės skirtingą svarbą klasifikuojant konkrečias EFS komponentes. Kiekvieno požymio svarbai nustatyti taikomas permutacinis požymių svarbos (FI) būdas [155]. Požymio j svarba yra apskaičiuojama lyginant pradinio modelio e^o ir modelio su permutuotomis reikšmėmis e^p paklaidą:

$$e^o = L(y, f(X)), \tag{3.5}$$



3.3 pav. Gradientinio tobulinimo sprendimų medžio algoritmo struktūra

$$e^p = L(y, f(X^p)), \tag{3.6}$$

čia X yra visų modelį sudarančių požymių rinkinys, o y yra anotacija (normalus arba nusilpęs). Funkcijos svarba FI_j reiškia klasifikavimo klaidos sumažėjimo dydį pašalinus požymio reikšmingumą. Atitinkamo požymio reikšmingumas pašalinamas sumaišius požymio vektoriaus vertes prieš išmokant mašininio mokymo algoritmą.

$$FI_j = \frac{e^{orig}}{e_j^p}. \tag{3.7}$$

Kiekvienos iš fiziologinių funkcijų FI EFS klasifikavimas vykomas randant funkciją reprezentuojančių požymių FI_j sumą.

Individualioms prognozėms interpretuoti naudojamas Shapley paaiškinimų metodas (SHAP). SHAP nurodo vidutinį klasifikavimo tikslumo pokytį, kai požymis įtraukiamas į algoritmo mokymą. Požymio j svarba įvertinama apskaičiuojant pridėtinę prognozės vertę ϕ kiekvienai m iteracijai, kai m = 1,...,M. Iteracijos susideda iš visų galimų X požymių derinių.

$$\phi_j^m = f(X_{+j}^m) - f(X_{-j}^m), \tag{3.8}$$

čia X_{+j} ir X_{-j} nurodo modelius, sudarytus su požymiu j ir be jo. Visų iteracijų pridėtinių prognozuojamų verčių vidurkis yra SHAP reikšmė.

$$\phi_j = \frac{1}{M} \sum_{m=1}^{M} \phi_j^m. \tag{3.9}$$

Fiziologinės funkcijos SHAP vertė yra tą fiziologinę funkciją charakterizuojančių požymių SHAP verčių suma.

4. REZULTATAI

4.1 Fizinių stresorių atpažinimo algoritmo tyrimas

Dinaminiu laiko skalės iškreipimu pagrįsto fizinių stresorių atpažinimo algoritmo tikslumo rezultatai pateikti 4.1 lentelėje. Algoritmu pasiekti geriausi rezultatai, kai naudojamas vertikalios ašies pagreičio signalas. Atpažįstant ėjimą Se yra 84,2 %, o PPV – 82,1 %. Atpažįstant lipimą laiptais Se yra 81,6 %, o PPV – 83,8 %.

4.1 lentelė. Fizinių stresorių atpažinimo algoritmo rezultatai, kai naudojamos skirtingos pagreičių signalų ašys

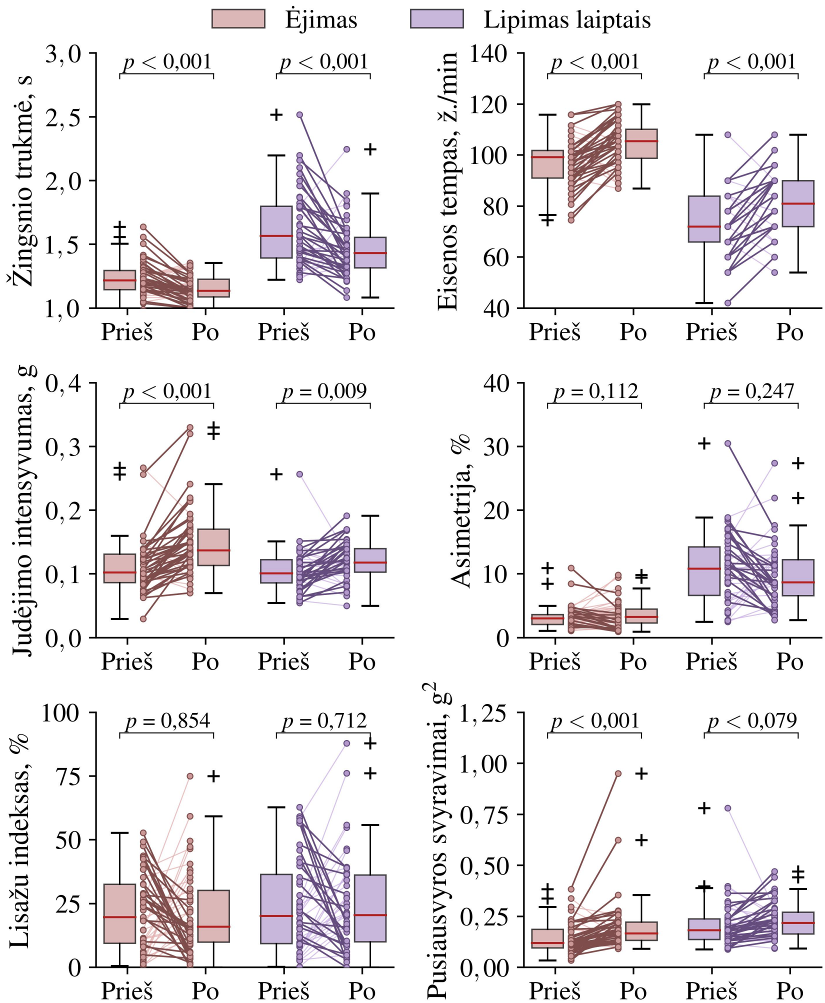
	Ėjimas		Lipimas laiptais		
	Se, %	PPV, %	Se, %	PPV, %	ACC
Priekinė-šoninė	95,1	69,5	57,9	93,6	76,9
Vidurio	75,0	68,7	65,8	72,5	70,4
Vertikali	84,2	82,1	81,6	83,8	82,9
Bendra amplitudė	97,4	65,5	46,7	94,9	73,0

4.2 Kinematinių parametrų tyrimas

Keturiasdešimt aštuoniems pacientams, kurie atliko 6-min ėjimo testą prieš ir po stacionarinės reabilitacijos, EFS įvertis vidutiniškai sumažėjo nuo 6,0 iki 4,7. Po stacionarinės reabilitacijos trys pacientai pagerino EFS įvertį keturiais balais, šeši – trimis, devyni – dviem ir spetyniolika – vienu balu. Parametrai nepagerėjo 11 pacientų, o dviem pablogėjo vienu balu. Veloergometrijos, 6-min ėjimo ir „stokis ir eik" testų rezultatai pagerėjo nuo 52,1 $\pm$ 18,3 W iki 61,3 $\pm$ 19,2 W ($p < 0,001$), nuo 301,1 $\pm 79,4$ m iki 387,2 $\pm$ 83,8 m ($p < 0,001$) ir nuo 8,3 $\pm$ 2,2 s iki 7,6 $\pm$ 1,7 s ($p = 0,017$). 4.1 pav. matyti, kad ėjimo metu visi kinematiniai parametrai, išskyrus eisenos asimetriją ir Lisažu indeksą, daugumai pacientų po stacionarinės reabilitacijos labai pagerėjo ($p < 0,001$). Tai yra žingsnio trukmė sumažėjo 34 (71 %) pacientams, ėjimo tempas padidėjo 37 (77 %), judėjimo intensyvumas padidėjo 40 (83 %), o pusiausvyros svyravimas padidėjo 39 (81 %). Padidėjęs pusiausvyros svyravimas gali būti paaiškintas didesniu judesių diapazonu dėl geresnės bendros fizinės būklės.

Keturiasdešimt keturiems pacientams, kurie atliko lipimo laiptais testą prieš ir po stacionarinės reabilitacijos, EFS įvertis vidutiniškai sumažėjo nuo 6,1 iki 4,6. Vienas pacientas pagerino EFS įvertį šešiais, vienas penkiais, trys keturiais, keturi trimis, du aštuoniais ir penkiolika – vienu balu. Dvylikai pacientų parametrai nepagerėjo. Veloergometrijos, 6-min ėjimo ir „stokis ir eik" testų rezultatai pagerėjo nuo 51,2 $\pm$ 16,3 W iki 62,0 $\pm$ 17,7 W ($p < 0,001$), nuo 298,7 $\pm 77,2$ m iki 380,9 $\pm$ 89,8 m ($p < 0,001$) ir atitinkamai nuo 8,4 $\pm$ 2,0 s iki 7,5 $\pm$ 1,8 s ($p = 0,008$). Kinematiniai parametrai lipimo laiptais testo metu pagerėjo mažiau nei ėjimo testo metu (4.1 pav).

Žingsnio trukmė sumažėjo 32 (73 %) ($p < 0,001$), eisenos tempas padidėjo 25 (57 %) ($p = 0,003$), o judėjimo intensyvumas padidėjo 28 (64 %) ($p = 0,009$).



4.1 pav. Kinematiniai parametrai įvertinti atliekant ėjimo ir lipimo laiptais testus prieš ir po stacionarinės reabilitacijos. Parametrų įverčiai su gerėjančia tendencija pavaizduoti storesne linija. p reikšmės apskaičiuotos taikant Wilcoxon signed-rank testą

Dauguma kinematinių parametrų nesiskyrė tarp intervencinės ir kontrolinės grupių prieš ir po treniruočių namuose, kas gerai atitinka reikšmingo skirtumo nebuvimą EFS įverčiuose (4.2 lentelė). EFS įvertis abiejose grupėse šiek tiek padidėjo, o tai rodo, kad nekontroliuojama sumažinto intensyvumo treniruočių programa nepagerino SSS būklės. Kiek netikėtai Lisažu indeksas padidėjo 13,1 % intervencinėje grupėje ir sumažėjo 5,14 % kontrolinėje grupėje ($p = 0,021$). Tai rodo padidėjusią judėjimo

4.2 lentelė. Kinematiniai ir funkcinio pajėgumo parametrai intervencinėje grupėje, kuri vykdė pratimų namuose programą, ir kontrolės grupėje, kuri laikėsi įprasto fizinio aktyvumo režimo

	Ėjimas		
	Intervencinė ($N = 18$)	Kontrolinė ($N = 11$)	p-vertė
Žingsnio greitis, s	-0,02 $\pm$ 0,17	-0,12 $\pm$ 0,21	0,342
Ėjimo tempas, ž./min	5,24 $\pm$ 9,70	7,45 $\pm$ 12,0	0,854
Judesių intensyvumas, g	0,03 $\pm$ 0,07	0,05 $\pm$ 0,06	0,538
Eisenos asimetrija, %	0,75 $\pm$ 3,81	-1,06 $\pm$ 3,26	0,129
Lisažu indeksas, %	13,1 $\pm$ 19,7	-5,14 $\pm$ 23,6	**0,021**
Svyravimai, g^2	0,07 $\pm$ 0,16	0,07 $\pm$ 0,09	0,582
Maksimalus pasiektas krūvis, W	7,07 $\pm$ 10,4	10,8 $\pm$ 7,82	0,205
6-min ėjimo atstumas, m	34,7 $\pm$ 84,5	49,3 $\pm$ 81,9	0,677
„Stokis ir eik“ trukmė, s	0,97 $\pm$ 2,96	0,71 $\pm$ 2,15	0,524
EFS įvertis	0,47 $\pm$ 1,77	0,00 $\pm$ 1,97	0,520
	Lipimas laiptais		
	Intervencinė ($N = 15$)	Kontrolinė ($N = 20$)	p-vertė
Žingsnio greitis, s	-0,04 $\pm$ 0,17	-0,07 $\pm$ 0,22	0,590
Ėjimo tempas, ž./min	1,67 $\pm$ 10,0	-3,27 $\pm$ 8,64	0,204
Judesių intensyvumas, g	0,01 $\pm$ 0,04	0,03 $\pm$ 0,02	**0,046**
Eisenos asimetrija, %	0,21 $\pm$ 4,59	-2,47 $\pm$ 8,48	0,982
Lisažu indeksas, %	-0,55 $\pm$ 24,5	-3,63 $\pm$ 30,0	0,840
Svyravimai, g^2	0,04 $\pm$ 0,06	-0,01 $\pm$ 0,07	0,051
Maksimalus pasiektas krūvis, W	6,00 $\pm$ 9,65	12,2 $\pm$ 10,0	0,149
6-min ėjimo atstumas, m	34,3 $\pm$ 70,4	39,9 $\pm$ 65,2	0,916
„Stokis ir eik“ trukmė, s	1,12 $\pm$ 2,63	0,88 $\pm$ 1,87	0,782
EFS įvertis	0,39 $\pm$ 1,72	0,27 $\pm$ 2,10	0,891

N nurodo pacientų skaičių grupėje.
Įverčių reikšmės nurodytos kaip vidurkis $\pm$ standartinis nuokrypis.
p-vertės yra įvertintos naudojant Kruskalio ir Walliso H-testą.

asimetriją tiems, kurie tęsė treniruotes. Lipimo laiptais metu judėjimo intensyvumas intervencinėje grupėje padidėjo 0,01 g, o kontrolinėje grupėje — 0,03 g ($p = 0,046$).

4.3 lentelėje pateikti kinematiniai parametrai pacientams, suskirstytiems į SSS, pažeidžiamus ir kuriems nėra SSS grupes, priklausomai nuo EFS įverčio. Skirtingos SSS būsenų grupės blogai atskiriamos remiantis kinematiniais parametrais, išskyrus lyginant SSS grupę su tų, kuriems nėra SSS, grupe. Ėjimo testo metu vidutinis ėjimo tempas, judėjimo intensyvumas ir pusiausvyros svyravimai buvo mažesni 6 žings/min ($p = 0,038$), 0,04 g ($p = 0,002$) ir 0,09 g^2 ($p = 0,021$) SSS grupėje, palyginti su grupe tų, kuriems nėra SSS. Lipimo laiptais testo metu SSS grupėje vidutinis ėjimo tempas buvo 9 žings/min ($p = 0,037$) mažesnis, palyginti su grupe tų, kuriems nėra SSS.

4.3 lentelė. Kinematiniai ir funkcinio pajėgumo parametrai skirtingose SSS grupėse, įvertinti atliekant ėjimo ir lipimo laiptais testus po stacionarinės reabilitacijos

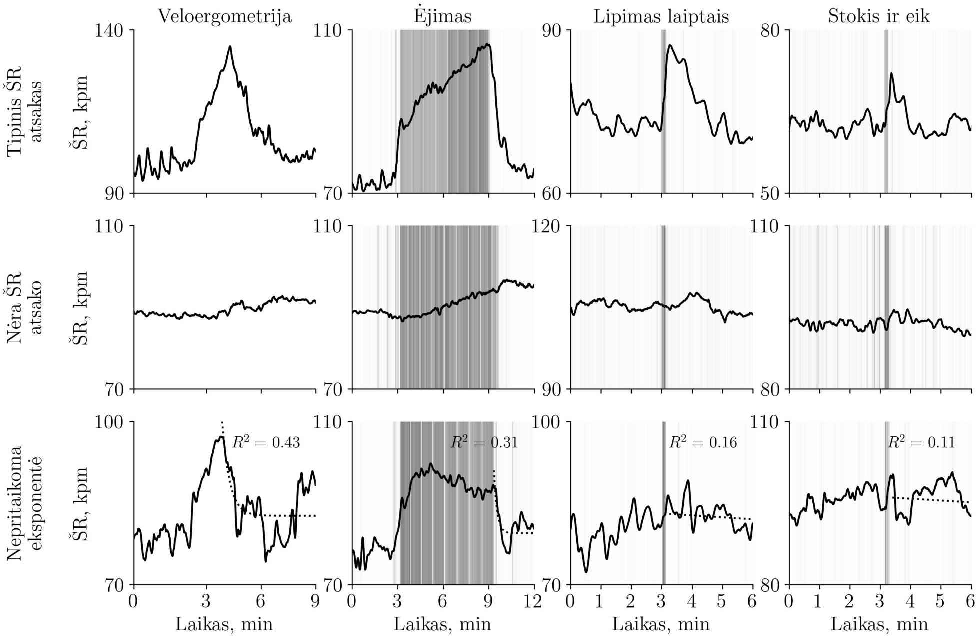
	Ėjimas			
	Nėra SSS (N = 18)	Pažeidžiami (N = 40)	SSS (N = 32)	p-vertė
Žingsnio greitis, s	1,20 ± 0,22	1,19 ± 0,14	1,24 ± 0,16	0,166
Ėjimo tempas, ž./min	103,1 ± 13,7	101,8 ± 11,2	97,6 ± 11,7	0,083
Judesių intensyvumas, g	0,16 ± 0,06	0,13 ± 0,05	0,12 ± 0,06	**0,005**
Eisenos asimetrija, %	4,02 ± 3,40	3,75 ± 2,40	4,12 ± 3,20	0,918
Lisažu indeksas, %	20,6 ± 13,3	21,4 ± 15,0	22,5 ± 17,1	0,976
Svyravimai, g^2	0,24 ± 0,21	0,16 ± 0,06	0,15 ± 0,06	**0,048**
Maksimalus pasiektas krūvis, W	64,9 ± 22,9	62,6 ± 23,2	53,5 ± 15,3	0,147
6-min ėjimo atstumas, m	416,4 ± 87,2	366,9 ± 112,4	322,4 ± 83,9	**0,002**
„Stokis ir eik“ trukmė, s	7,00 ± 1,18	7,75 ± 1,50	8,92 ± 2,19	**0,004**
EFS įvertis	2,56 ± 0,62	4,45 ± 0,50	7,34 ± 1,18	<**0,001**
	Lipimas laiptais			
	Nėra SSS (N = 16)	Pažeidžiami (N = 32)	SSS (N = 35)	p-vertė
Žingsnio greitis, s	1,46 ± 0,27	1,54 ± 0,27	1,64 ± 0,35	0,143
Ėjimo tempas, ž./min	82,1 ± 12,1	77,6 ± 12,6	73,2 ± 13,4	0,097
Judesių intensyvumas, g	0,12 ± 0,04	0,11 ± 0,03	0,11 ± 0,04	0,384
Eisenos asimetrija, %	9,33 ± 4,51	10,4 ± 4,91	10,8 ± 5,31	0,648
Lisažu indeksas, %	22,2 ± 21,4	25,8 ± 21,7	23,8 ± 14,6	0,675
Svyravimai, g^2	0,23 ± 0,08	0,21 ± 0,08	0,20 ± 0,09	0,268
Maksimalus pasiektas krūvis, W	65,3 ± 19,8	61,3 ± 19,5	52,7 ± 15,3	**0,047**
6-min ėjimo atstumas, m	402,6 ± 76,7	359,1 ± 97,9	313,0 ± 85,7	**0,002**
„Stokis ir eik“ trukmė, s	6,78 ± 0,98	7,78 ± 1,65	9,14 ± 2,80	**0,002**
EFS įvertis	2,69 ± 0,48	4,34 ± 0,48	7,11 ± 1,13	<**0,001**

Pacientai suskirstyti į grupes pagal SSS stadiją: ⩽3 — nėra SSS, 4–5 — pažeidžiami, ⩾6 — SSS [159].
N nurodo pacientų skaičių grupėje.
Įverčių reikšmės nurodytos kaip vidurkis ± standartinis nuokrypis.
p-vertės yra įvertintos naudojant Kruskalio ir Walliso H-testą.

4.3 Širdies ritmo atsako įvertinimo parametrų tyrimas

Netinkamos ŠR sekos, pvz., tos, kuriose nėra ŠR atsako į fizinį stresorių arba kurių normalizavimosi fazėje matomas didelis ŠR varijavimas, neįtrauktos į analizę. ŠR atsako nebuvimu laikomos ŠR sekos, kai fizinio stresoriaus poveikio metu ritmas pakyla mažiau nei 5 kpm, palyginti su ramybės ŠR. Ryškiu ŠR varijavimu, kurį sukėlė fiziologiniai veiksniai arba nenumatyta pacientų veikla (pvz., pasisukimas, svyravimai), laikomos ŠR sekos, kurioms eksponentės pritaikymo prie ŠR normalizavimosi fazės determinacijos koeficientas gautas mažesnis už fiksuotą slenkstį 0,5. Tipinių bei netinkamų analizei ŠR sekų pavyzdžiai kiekvieno fizinio stresoriaus atveju pateikti 4.2 pav.

4.3 pav. pateiktas ryšys tarp ŠR atsako parametrų, įvertintų veloergometrijos testo ir kasdienės veiklos stresorių metu. Visi ištirti kasdienės veiklos stresoriai rodo

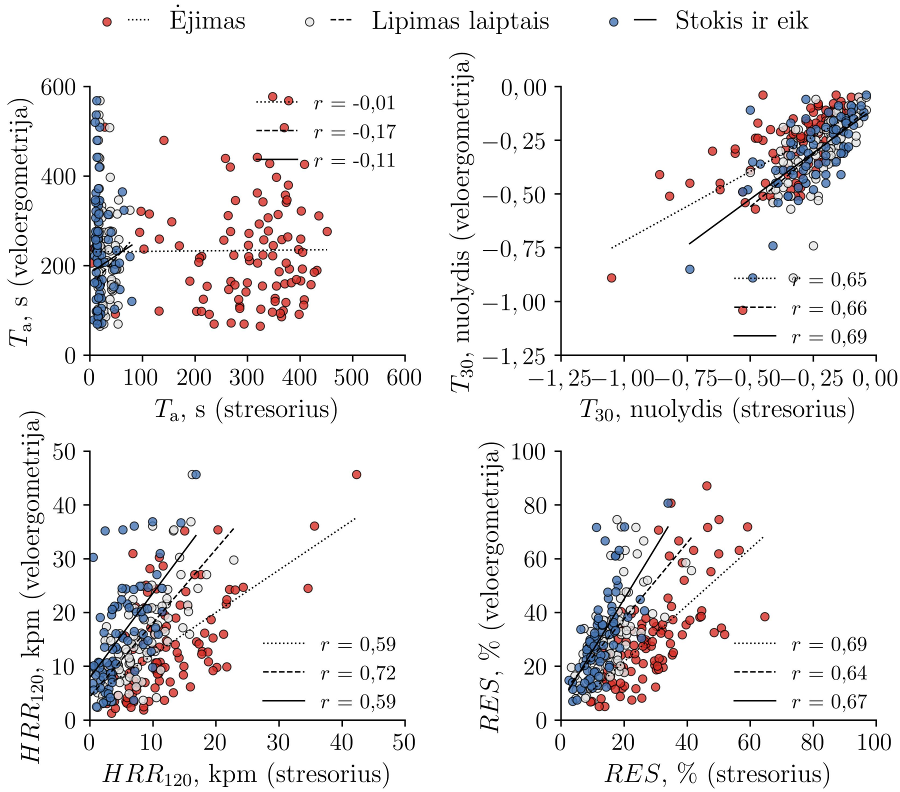


4.2 pav. Tipinių ir analizei netinkamų ŠR sekų pavyzdžiai fizinių stresorių metu. Pilkos juostos žymi fizinio aktyvumo intensyvumą, įvertintą vidutiniu absoliučiu pagreičio signalo nuokrypiu. Pastaba: fizinio aktyvumo intensyvumo pagreičio signaluose nebuvo galima įvertinti veloergometrijos metu dėl sėdėjimo ant dviračio ergometro

vidutinę ar didelę koreliaciją lyginant ŠR atsako parametrus T_{30} ir HRR_{120} bei ŠR rezervą. Kita vertus, nė vienas iš kasdienės veiklos stresorių nesukėlė panašių ŠR augimo fazės tendencijų kaip atliekant veloergometriją, todėl T_{a} parametras reikšmingai nekoreliavo.

4.4 pav. rodo ryšį tarp ŠR atsako ir ramybės ŠR parametrų, suskirstytų į kvartilius, bei SSS būklės įvertinimų. Ryšys akivaizdus tarp ŠR atsako parametrų pablogėjimo ir SSS būklės pablogėjimo, kurį indikuoja didėjantis EFS įvertis. Ramybės ŠR apibūdinantys parametrai, t. y. ŠR ramybės metu, SampEn ir SDNN, rodo tą pačią tendenciją iki aukščiausio kvartilio.

Siekiant ištirti stacionarinės reabilitacijos poveikį ŠR atsakui ir ramybės ŠR, parametrai apskaičiuoti prieš ir po reabilitacijos, atliekant veloergometriją ir kasdienės veiklos stresorių metu. Veloergometrijos, ėjimo, lipimo laiptais ir „stokis ir eik“ testai prieš ir po stacionarinės reabilitacijos atlikti 41, 29, 26 ir 18 pacientų. ŠR atsako parametrai reikšmingai pasikeitė tik veloergometrijos testo metu: T_{a} padidėjo nuo 175$\pm$84 s iki 242$\pm$78 s ($p < 0,05$), T_{30} sumažėjo nuo -0,21$\pm$0,12 iki -0,29$\pm$0,14 ($p < 0,05$), HRR_{120} padidėjo nuo 10,6$\pm$6,2 kpm iki 13,9$\pm$7,3 kpm ($p < 0,05$) ir RES padidėjo nuo 23,3$\pm$11,3 % iki 29,2$\pm$14,6 % ($p = 0,05$). Reikšmingų parametrų pokyčių ėjimo, lipimo laiptais ir „stokis ir eik“ testų metu nebuvo.

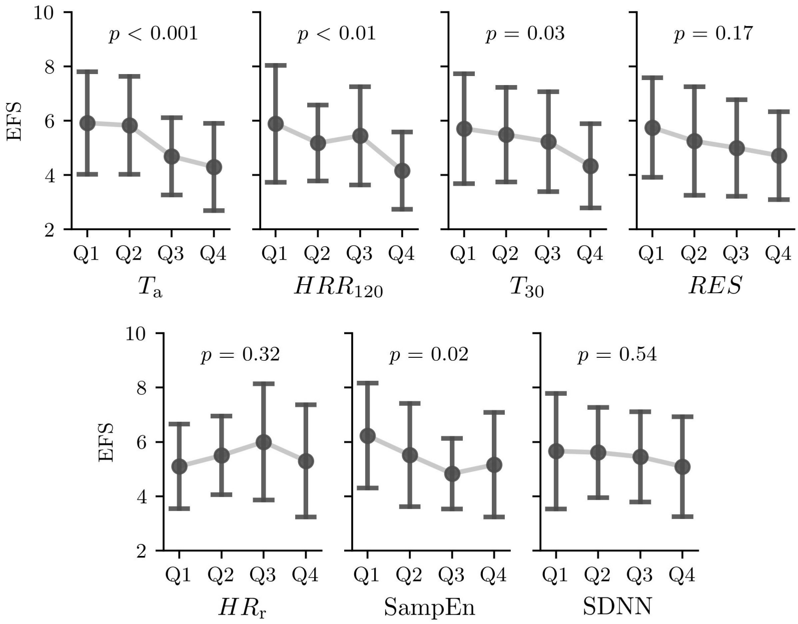


4.3 pav. Ryšys tarp ŠR atsako parametrų veloergometrijos testo ir kasdienės veiklos stresorių metu. Pateikiamos koreliacijos pagal duomenis, gautus prieš stacionarinę reabilitaciją, po stacionarinės reabilitacijos ir po treniruočių namuose

4.5 pav. parodytas visos treniruočių programos poveikis ŠR atsako parametrams intervencijos ir kontrolės grupėse. Veloergometrijos, ėjimo, lipimo laiptais ir „stokis ir eik“ testai, kurie apėmė visą treniruočių programą, buvo atlikti atitinkamai 30, 25, 22 ir 15 pacientų. Visi ŠR atsako parametrai, išskyrus T_a, reikšmingai pagerėjo kontrolinei grupei veloergometrijos metu ($p < 0,05$).

Lyginant kasdienės veiklos stresorius su veloergometrija, parametrų tendencijas labiausiai atitiko ėjimo stresorius, o lipimo laiptais ir „stokis ir eik“ stresoriai yra mažiau tinkami parametrų pokyčiams stebėti.

Reikšmingų skirtumų nepastebėta ŠR atsako parametruose prieš ir po visos treniruočių programos tarp intervencinės ir kontrolinės grupių, išskyrus T_a lipimo laiptais stresoriaus metu. Skirtumų nebuvimas atitinka EFS įvertį pasibaigus visai treniruočių programai intervencinėje (4,13 $\pm$ 1,45) ir kontrolinėje (4,78 $\pm$ 1,66) grupėse.



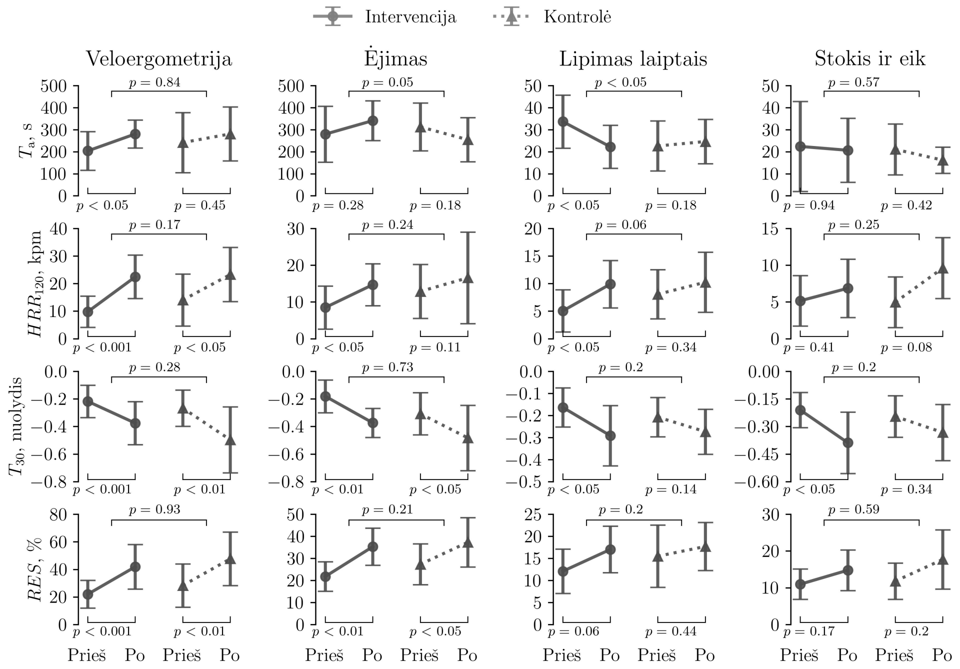
4.4 pav. SSS būklės įvertinimai ŠR atsako į veloergometrijos testą ir ramybės ŠR parametrų kvartiliuose. Rezultatai pateikiami vidurkiu±standartiniu nuokrypiu naudojant duomenis, gautus prieš stacionarinę reabilitaciją, po stacionarinės reabilitacijos ir po treniruočių namuose. p vertė apskaičiuota EFS balų kitimo tendencijoms atitinkamuose ŠR parametrų kvartiliuose

4.4 Nusilpusių komponenčių identifikavimo algoritmo tyrimas

4.4 lentelė lentelėje pateikiami gradientinio tobulinimo sprendimų medžio modelio, sukurto naudojant klinikinius ir dėvimais įrenginiais išskirtus požymius, klasifikavimo rezultatai. Modelio tikslumas, įvertinamas F_1 įverčiu, yra 77,8 % ir 72,7 % klasifikuojant bendrą sveikatos būklę, 71,3 % ir 65,3 % – funkcinį savarankiškumą, 72,6 % ir 76 % – mitybą, ir 84,7 % ir 81,0 % – funkcinę būklę, atitinkamai naudojant klinikinius ir dėvimais įrenginiais išskirtus požymius.

4.4 lentelė. Modelio, išmokyto klinikiniais požymiais ir požymiais, išskirtais iš dėvimais įrenginiais registruojamų biosignalų, klasifikavimo įvertinimas. Modelio klasifikavimas įvertintas F_1 įverčiu

EFS komponentė	Klinikiniai įverčiai	Dėvimais įrenginiais išskirti įverčiai
Bendroji sveikatos būklė	77.8%	72.7%
Funkcinis savarankiškumas	71.3%	65.3%
Mityba	72.6%	76.0%
Funkcinė būklė	84.7%	81.0%

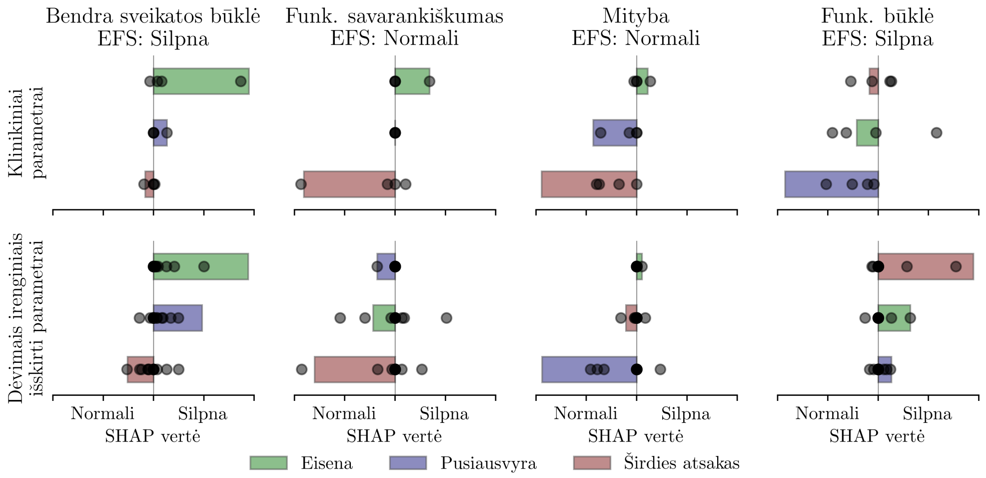


4.5 pav. Visos treniruočių programos poveikis ŠR atsako parametrams intervencijos ir kontrolinėse grupėse. p vertė kiekvienos dalies viršuje apibūdina parametrų pokytį prieš ir po visos treniruočių programos intervencinėje ir kontrolinėje grupėse. p vertės kiekvienos dalies apačioje apibūdina parametrų pokytį prieš ir po visos treniruočių programos intervencinėje ir kontrolinėje grupėse

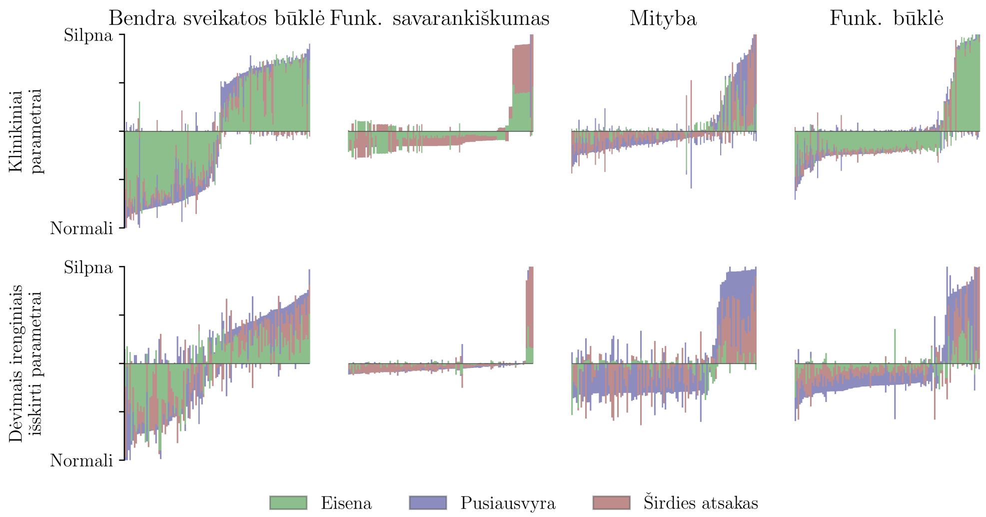
4.6 pav. pateikiama vieno paciento nusilpusių funkcijų identifikavimo modelio sprendimų interpretacija. Pateiktame pavyzdyje klinikiniai ir dėvimais įrenginiais išskirti požymiai panašiai prisidėjo klasifikuojant bendrą sveikatos būklę, funkcinį savarankiškumą ir mitybos EFS komponentes, tačiau jų indėlis buvo priešingas klasifikuojant funkcinės būklės komponentę.

4.7 pav. parodytas visų pacientų SHAP reikšmių pasiskirstymas. Klinikiniai ir dėvimais įrenginiais išskirti požymiai rodė panašias tendencijas klasifikuojant bendrą sveikatos būklę, funkcinį savarankiškumą ir mitybos EFS komponentes, tačiau identifikuojant funkcinę būklę prisidėjo skirtingos fiziologinės funkcijos.

Tam tikra fiziologinė funkcija identifikuojama kaip nusilpusi, kai ji daugiausiai prisideda prie klasifikavimo. Rezultatai rodo, kad dėvimais įrenginiais išskirtais požymiais pagrįsta nusilpusios EFS komponentės klasifikavimo prognozė visais atvejais, išskyrus funkcinės būklės, sutampa su klinikiniais požymiais pagrįstu klasifikavimu. Klasifikuojant bendrąją sveikatos būklę, eiseną ir pusiausvyrą charakterizuojantys požymiai rodė komponentės nusilpimą atitinkamai 47,9 % ir 35,5 % pacientų. Klasifikuojant funkcinį savarankiškumą, ŠR atsakas buvo pagrindinis veiksnys 81,8 % pacientų.



4.6 pav. Konkretaus paciento EFS komponenčių klasifikavimo interpretavimas SHAP būdu



4.7 pav. Visų pacientų interpretavimo rezultatų palyginimas ir atskirų funkcijų svarbos klasifikuojant palyginimas

IŠVADOS

1. Pasiūlytas ir ištirtas dinaminiu laiko skalės iškreipimu pagrįstas algoritmas, skirtas aptikti ėjimą ir lipimą laiptais dėvimais įrenginiais užregistruotuose biosignaluose. Atpažįstant ėjimą pasiektas 84,2 % jautrumas ir 82,1 % teigiama prognostinė vertė, o lipimą laiptais — 81,6 % jautrumas ir 83,8 % teigiama prognostinė vertė. Fizinių stresorių atpažinimas kasdienėje veikloje atveria galimybes įvertinti širdies ritmo reakciją į fizinius stresorius.

2. Tyrimai parodė, kad SSS progresavimo tendencijos stebėsena reabilitacijos metu, remiantis kinematiniais parametrais, gautais iš dėvimais įrenginiais registruojamų biosignalų, yra įmanoma. Dauguma kinematinių parametrų, įvertintų ėjimo testo metu, pagerėjo po reabilitacijos: žingsnio trukmė, ėjimo tempas, pusiausvyros svyravimai ir judesių intensyvumas pagerėjo 71 %, 77 %, 81 % ir 83 % pacientų. O kinematiniai parametrai lipimo laiptais testo metu pagerėjo mažiau. Po treniruočių namuose programos reikšmingų kinematinių parametrų pokyčių nepastebėta, o tai atitinka nedidelį SSS būklės pablogėjimą. Kinematinių parametrų stebėsena vaikščiojant ir lipant laiptais gali būti naudinga vertinant treniruočių programų efektyvumą SSS pacientams.
3. Siekiant visapusiškai apibūdinti širdies ritmo atsaką, pasiūlyti parametrai, charakterizuojantys širdies ritmo greitėjimo ir lėtėjimo fazes ir visą širdies ritmo atsako fazę. Atliekant kasdienės veiklos stresorius imituojančius testus (ėjimo, lipimo laiptais ir „stokis ir eik“), širdies ritmo atsako ir širdies ritmo rezervo parametrai vidutiniškai koreliavo (r = 0,59–0,72) su analogiškais parametrais, įvertintais veloergometrijos testo metu. Remiantis tyrimo rezultatais, kasdienėje veikloje rekomenduojama vertinti širdies ritmo atsaką į ėjimą.
4. Pasiūlyta interpretuojamo mašininio mokymosi algoritmo koncepcija, skirta identifikuoti kliniškai informatyviems požymiams, suteikiantiems informacijos apie nusilpusias paciento fiziologines funkcijas. Algoritmo patikimumas įvertintas F_1 įverčiu, kuris yra 77,8 % ir 72,7 % klasifikuojant bendrąją sveikatos būklę, 71,3 % ir 65,3 % funkcinį savarankiškumą, 72,6 % ir 76 % mitybą ir 84,7 % ir 81,0 % funkcinę būklę, naudojant klinikinius ir dėvimais įrenginiais registruojamus požymius.

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CURRICULUM VITAE

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Qualifications:
Bachelor of Biomedical Electronics, Kaunas University of Technology (2012 - 2016), Master of Biomedical Engineering, Kaunas University of Technology (2016 - 2018), PhD in Electrical and Electronics Engineering, Biomedical Engineering Institute, Kaunas University of Technology (2019 - 2023), PhD topic "Methods for unobtrusive monitoring of heart response to physical stressors in activities of daily living."
Supervisor: Andrius Petrėnas

Employment history:
Junior Researcher, Biomedical Engineering institute, Kaunas University of Technology (2019 - present), Engineer, Biomedical Engineering institute, Kaunas University of Technology (2017 - 2020), Automation Engineer, "Vakarų medienos grupė" (2016 - 2017), Project Engineer, Biomedical Engineering institute, Kaunas University of Technology (2016 - 2017).

Research:
Frailty severity assessment: I am currently developing methods to estimate the severity of frailty progression in elderly patients. Methods are based on data acquired from wearable devices. Study is done with the intention to apply machine learning techniques for outcome prediction.
Assessment of functional performance in free-living: I am working on algorithms to estimate functional performance of cardiovascular and multiple sclerosis patients. Methods are based on continuous physical activity measurements. Working in collaboration with *BsiCos* research group of Zaragoza University, Zaragoza, Spain.
Mental stress monitoring: I have developed and tested methods to monitor mental stress. Developed methods were based on data acquired from wearable sensors. Methods were used to estimate the mental stress of managers during stressful situations. Preliminary research was done in collaboration with company *Inlusion Netforms*. Methods were used for a multimodal deep learning-based application.
Atrial fibrillation monitoring: I am working on development of methods of atrial fibrillation screening. My work includes signal processing, data collection and software development. Study is done in collaboration with Santara Clinics, Vilnius, Lithuania.

LIST OF PUBLICATIONS ON THE SUBJECT OF THE DOCTORAL THESIS

Publications in the journals referred in the *Clarivate Analytics Web of Science* database with impact factor

1. **Sokas, Daivaras**; Tamulevičiūtė-Prascienė, Eglė; Beigienė, Aurelija; Barasaitė, Vitalija; Marozas, Julius; Kubilius, Raimondas; Bailón, Raquel; Petrėnas, Andrius. Wearable-based assessment of heart rate response to physical stressors in patients after open-heart surgery with frailty. *IEEE Journal of Biomedical and Health Informatics*. 2023, vol. 27, iss. 4, p. 1825-1834. [IF: 7.021, Q1, 2021]

2. Butkuvienė, Monika; Tamulevičiūtė-Prascienė, Eglė; Beigienė, Aurelija; Barasaitė, Vitalija; **Sokas, Daivaras**; Kubilius, Raimondas; Petrėnas, Andrius. Wearable-based assessment of frailty trajectories during cardiac rehabilitation after open-heart surgery. *IEEE Journal of Biomedical and Health Informatics*. 2022, vol. 26, iss. 9, p. 4426-4435. [IF: 7.021, Q1, 2021]

3. Bacevicius, Justinas; Abramikas, Zygimantas; Dvinelis, Ernestas; Audzijoniene, Deimile; Petrylaite, Marija; Marinskiene, Julija; Staigyte, Justina; Karuzas, Albinas; Juknevicius, Vytautas; Jakaite, Rusne; Basyte-Bacevice, Viktorija; Bileisiene, Neringa; Solosenko, Andrius; **Sokas, Daivaras**; Petrenas, Andrius; Butkuviene, Monika; Paliakaite, Birute; Daukantas, Saulius; Rapalis, Andrius; Marinskis, Germanas; Jasiunas, Eugenijus; Darma, Angeliki; Marozas, Vaidotas; Aidietis, Audrius. High specificity wearable device with photoplethysmography and six-lead electrocardiography for atrial fibrillation detection challenged by frequent premature contractions: DoubleCheck-AF. *Frontiers in Cardiovascular Medicine*. 2022, vol. 29, iss. 4, p. 1-11. [IF: 5.848, Q2, 2021]

4. **Sokas, Daivaras**; Paliakaitė, Birutė; Rapalis, Andrius; Marozas, Vaidotas; Bailón, Raquel; Petrėnas, Andrius. Detection of walk tests in free-living activities using a wrist-worn device. *Frontiers in Physiology*. 2021, vol. 12, art. No. 706545, p. 1-13. [IF: 4.755, Q1, 2021]

Publications referred in the *Clarivate Analytics Web of Science* database without impact factor

1. **Sokas, Daivaras**; Rapalis, Andrius; Petrėnas, Andrius; Daukantas, Saulius; Marozas, Vaidotas. Evaluation of stair climbing as an approach for estimating heart rate recovery in daily activities. *BIOSTEC 2021: Proceedings of the 14th International Joint Conference on Biomedical Engineering Systems and Technologies. Vol 4. Biosignals*. 2021, vol. 4, p. 21-25.

2. Patašius, Martynas; Šimkienė, Jūratė; **Sokas, Daivaras**; Pranskūnas, Andrius. Method for finding the limits of blood vessel landmarks in eye fundus images based on distances in graphs: preliminary results. *IFMBE proceedings: Medicon 2019: XV Mediterranean Conference on Medical and Biological Engineering and Computing, September 26-28, 2019, Coimbra, Portugal: conference proceedings*. 2019, vol. 76, p. 358-366.

Conference presentation abstracts

1. **Sokas, Daivaras**. Išsėtinės sklerozės pacientų fizinės negalios vertinimas panaudojant išmaniąją apyrankę. *Bioateitis: gamtos ir gyvybės mokslų perspektyvos: 15-oji Lietuvos jaunųjų mokslininkų konferencija: pranešimų tezės*. 2022. p. 40.

2. **Sokas, Daivaras**. Širdies ritmo, užlipus laiptais, atsistatymo vertinimas naudojant išmaniąją apyrankę. *Bioateitis: gamtos ir gyvybės mokslų perspektyvos: 12-oji jaunųjų mokslininkų konferencija: programa ir pranešimų santraukos*. 2019. p. 27.

List of attended conferences

1. **Sokas, Daivaras**. Išsėtinės sklerozės pacientų fizinės negalios vertinimas panaudojant išmaniąją apyrankę. *Bioateitis: gamtos ir gyvybės mokslų perspektyvos: 15-oji Lietuvos jaunųjų mokslininkų konferencija: pranešimų tezės*: 24 November 2022, Vilnius, Lithuania.

2. **Sokas, Daivaras**; Rapalis, Andrius; Petrenas, Andrius; Daukantas, Saulius; Marozas, Vaidotas. Evaluation of stair climbing as an approach for estimating heart rate recovery in daily activities. *BIOSTEC 2021: 14th International Joint Conference on Biomedical Engineering Systems and Technologies*: 11-13 February 2021.

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Open access databases

1. **Sokas, Daivaras**; Butkuvienė, Monika; Tamulevičiūtė-Prascienė, Eglė; Beigienė, Aurelija; Kubilius, Raimondas; Petrėnas, Andrius; Paliakaitė, Birutė. Wearable-based signals during physical exercises from patients with frailty after open-heart surgery (version 1.0.0). *Physionet*, 2022.

2. Bacevičius, Justinas; Abramikas, Žygimantas; Badaras, Ignas; Butkuvienė, Monika; Daukantas, Saulius; Dvinelis, Ernestas; Gudauskas, Modestas; Jukna, Edvardas; Kiseliūtė, Margarita; Kundelis, Ričardas; Marinskienė, Julija; Paliakaitė, Birutė; Petrėnas, Andrius; Petrylaitė, Marija; Pilkienė, Aistė; Pluščiauskaitė, Vilma; Rapalis, Andrius; **Sokas, Daivaras**; Sološenko, Andrius; Staigytė, Justina; Stankevičiūtė, Guostė; Taparauskaitė, Neringa; Aidietis, Audrius; Marozas, Vaidotas. Long-term electrocardiogram and wrist-based photoplethysmogram recordings with annotated atrial fibrillation episodes. *Zenodo*, 2022.

UDK 004.891.13+612.67] (043.3)

SL 344. 2023-xx-xx, xx,xx leidyb. apsk. 1. Tiražas 14 egz. Užsakymas xxx.
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