DISSERTATION

Relationships between lifestyle and transient cardiovascular response in hip operated patients compared to a control group

Submitted by

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in Heaven

Dedicated to my so beloved family

on Earth

STATUTORY DECLARATION

I hereby declare that this thesis is my own original work and that I have fully acknowledged by name all of those individuals and organizations that have contributed to the research for this thesis. Due acknowledgement has been given in the text to all other material used. Throughout this thesis and in all related publications I followed the "Standards of Good Scientific Practice" and Ombuds Committee at the Medical University of Graz.

Graz, 4.3.2022

Regina Csanády-Leitner

DISCLOSURES

Copyright Statements

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All co-authors have explicitly agreed to the use of the published data in this thesis.

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PUBLICATIONS

The following publications and conference contributions have been completed over the course of the doctoral program.

(1) Csanády-Leitner R., Lackner H.K., Maurer-Ertl W., Seibert F.J. Hip fracture in older age caused by a decline of cognitive and cardiovascular functions. 13th EUGMS in Nice/France, September 20/22, 2017.

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ABBREVIATIONS AND DEFINITIONS

ANOVA	Analysis of Variance
ANS	Autonomic nervous system
BMI	Bodymass Index
Bpm	Beats per minute
°C	Degree Celsius
CC	Calf circumference
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
EDF	European data format
F – value	A statistical value of the ANOVA, describing the variance between the means of two populations
FD	Frequency domain
Fig	Figure
GS	Grip strength
HF	High frequency, Power of the "high" frequency band, 0.15–0.4 Hz
HFS	Hip fracture surgery
HR	Heart rate
HRV	Heart rate variability
Hz	Hertz
Kinetic b	Kinetic behavior
LF	Low frequency, Power of the "low" frequency band, 0.04–0.15 Hz
LF/HF	Ratio between LF and HF
ln	Natural logarithm
ms	Milliseconds
NN	Time between two successive heartbeats; N means normal
OECD	Organisation for Economic Co-operation and Development
PC	Personal computer
PNS	Parasympathetic nervous system
PSD	Power spectral density

p – value	Significance testing of a result to the null hypothesis
RMSSD	Root mean square standard deviation of N-N intervals
RSA	Respiratory sinus arrhythmia
SBP	Systolic blood pressure
SDNN	Standard deviation of N-N interval time series
SEDENTARY b	Sedentary behavior
SNS	Sympathetic nervous system
SPSS	Statistical package for the social science
TD	Time domain
THA	Total hip arthroplasty
Tukey´s–HSD Test	Tukey´s – honestly significant difference test – post hoc test for multiple comparisons
VLF	Very low frequency
$ή^2$	Eta squared – a measure of effect size for use in ANOVA models

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ABSTRACT IN GERMAN

Hintergrund

In der westlichen Welt treten vielfach Gesundheitsprobleme, wie z.B. Herz-Kreislauf oder chronische Erkrankungen auf, die im Lebensstil einer Person ihren Ursprung haben können. Ein probates Mittel den aktuellen Gesundheitszustand einfach und kostengünstig abzuschätzen ist die Analyse der Herzfrequenzvariabilität. Die Möglichkeit eines Zusammenhangs zwischen Lebensstil und Herzfrequenzvariabilität kann für eine Risikoabschätzung genützt werden. Bislang gibt es noch unzureichend Studien, die diesen Zusammenhang insbesondere bei Personen mit Hüftoperationen untersuchen. Um diese Lücke zu schließen, werden in der vorliegenden Studie Zusammenhänge von Lebensstil und kardiovaskulären Parametern zwischen Patienten nach Hüftoperationen und einer Kontrollgruppe untersucht.

Methoden

71 Teilnehmer (40 Frauen) im Alter von 60-85 Jahren wurden in diese Studie eingeschlossen und bildeten drei Gruppen – Patienten nach Hüftoperationen (21 Hüftfrakturen und 30 Hüftendoprothesen) und eine Kontrollgruppe (20 Teilnehmer). Während der gesamten Aufzeichnung des Elektrokardiogramms wurden die Griffkraft und der STROOP-Test als Stressoren angewendet. Daten von Ausgangs- und Erholungsphasen wurden ausgewertet. Um die Veränderung kardiovaskulärer Parameter in den Studiengruppen zu erkennen und zu analysieren, wurde eine ANOVA mit wiederholten Messungen verwendet. Zusätzlich wurden Daten von Lebensstilfaktoren und kardiovaskulären Faktoren mit einer Pearson-Korrelation analysiert und durch die Anwendung einer logistischen Regression konnten Prädiktoren für den STROOP3-Test identifiziert werden.

Ergebnisse

Ergebnisse der Analyse zu den Baseline-HRV-Parametern zeigten signifikante Unterschiede in HR, *ln*SDNN, *ln*LF und *ln*HF. Zusätzlich konnte ein Interaktionseffekt im Parameter *ln*SDNN zwischen der HFS- und der Kontrollgruppe gefunden werden. Die Korrelationsanalyse zeigte schwache bis mäßige Korrelationen zwischen HRV und Lebensstilparametern. Abschließend zeigte die logistische Regression der STROOP3-Variablen signifikante Unterschiede zwischen der HFS- und THA-Gruppe sowie zwischen der HFS- und Kontrollgruppe.

Schlussfolgerung

Lebensstil und kardiovaskuläre Parameter zeigten Unterschiede zwischen den Gruppen. Dies lässt den Schluss zu, dass durch nicht invasive Messungen gesundheitliche Defizite, die durch Lebensstil bedingte Aspekte entstehen, frühzeitig erkannt werden und daraus präventive Maßnahmen abgeleitet werden können. Daher kann diese Studie möglicherweise neue Einblicke in die Forschung und deren Fragen zu Lebensstil von hüftoperierten älteren Menschen geben und so eine Literaturlücke mit dem Hauptinteresse an den Beziehungen zwischen Lebensstil und HRV bei hüftoperierten Patientengruppen im Vergleich zu einer Kontrollgruppe schließen.

Schlüsselwörter: Hüftfraktur, Hüftendoprothetik, kardiovaskuläre Reaktivität, Herzfrequenzvariabilität, Alterungsprozess

ABSTRACT IN ENGLISH

Background

In the western world, many health problems such as cardiovascular or chronic diseases can originate from a person's lifestyle. An effective means of proving the current state of health simply and cost-efficiently is the analysis heart rate variability. Accordingly, the possibility of a connection between lifestyle and heart rate variability can be used for risk assessment. To date, there are still insufficient studies examining this relationship, especially in people who have had hip operations. In order to close this gap, the aim of the present study is to examine the relationships between lifestyle and cardiovascular parameters between patients after hip surgery compared with a control group.

Methods

Seventy-one participants (40 women) aged 60-85 years were included in this study and formed three groups: patients after hip operations (21 hip fractures and 30 hip replacements) and a control group (20 participants). Grip strength and the STROOP test were used as stressors throughout the recording of the electrocardiogram. Data from the initial and recovery phases were evaluated. A repeated measures ANOVA was used to identify and analyze changes in cardiovascular parameters in the study groups. In addition, data on lifestyle factors and cardiovascular factors with a Pearson correlation were analyzed and predictors for the STROOP3 test could be identified using logistic regression.

Results

Results of the analysis on the baseline HRV parameters indicated significant differences in HR, *In*SDNN, *In*LF and *In*HF. In addition, an interaction effect could be found between the HFS and the control group in the *ln*SDNN parameter. Correlation analysis showed weak to moderate correlations between HRV and lifestyle parameters. Finally, the logistic regression of the STROOP3 variables presented significant differences between the HFS and THA groups and between the HFS and control groups.

Conclusions

Lifestyle and cardiovascular parameters showed differences between the groups. This prompts the conclusion that non-invasive measurements can be used to identify health deficits caused by lifestyle-related aspects at an early stage and derive preventive measures accordingly.

Therefore, this study can provide new insights into the research and lifestyle issues of hip-operated elderly people, closing a literature gap with the main interest in the relationship between lifestyle and HRV in hip-operated patient groups compared with a control group.

Keywords: Hip fracture, Total hip arthroplasty, Cardiovascular reactivity, Heart rate variability, Aging

1 INTRODUCTION

A major change in demographic structure has been recognized since the 19th century in almost all industrial countries, including Austria. A decline in the proportion of people aged between 20 to 64 years has been observed and is expected to continue, whereas the percentage of people over 64 years old is steadily increasing [1]. Indeed, an increase of those in this age group from 18 percent to 24 percent is forecasted for 2030 [2]. This leads to an imbalance in the population structure. In this context, the health system is challenged to find preventive approaches that promote an independent and self-determined life for those in this population group, in order to prevent a financial explosion of hospital costs [3]. An important aspect of such approaches relates to the personal choice of lifestyle, which influences one's life as well as the overall public health situation [4]. Numerous articles have been written on this important topic, with issues promoting a better lifestyle and a self-responsible way of dealing with a personal health situation [5, 6]. Sánchez-Garcia et al. stated that monitoring and improving the health status of older individuals takes – besides genetics and dietary – socio-demographic and lifestyle factors into account [7]. In particular, lifestyle factors like mobility, physical activity and body mass index (BMI) as well as weight and underweight plus BMI have a high incidence and risk of hip fractures, followed by inactivity, high coffee consumption, weight loss and daily high alcohol consumption [8, 9].

1.1 LIFESTYLE AND SOCIO-DEMOGRAPHIC FACTORS

Originally, the term lifestyle was used in research and the media to define health and the manner or way of living [10]. Values and attitudes are unconsciously carried over from the older generation and influenced by cultural milieus as well as media and globalization, whereby the pluralistic way of lifestyle draws a picture through which an individual can express oneself [11]. Different levels have been observed defining a concept of lifestyle, namely how to live one's life [12]. Daily habits have an enormous impact on short- as well as long-term health, influencing one's quality of life [13]. Evidence-based guidelines underscore the impact of daily habits and actions as being important for the prevention and treatment of diseases like regular physical activity, body weight, nutrition, cigarette smoking, sedentary behavior, eye disease and activity levels, as examples among a widespread number of possibilities essentially influencing health positively as well as negatively [14–16]. Socio-demographic variables are known to influence people's attitudes towards healthy lifestyle behaviors including age, gender, income and social networking [17]. The importance of daily habits with a possible influence on the prevention or treatment of diseases or therapies and the focus set on lifestyle and its relationship with health and the implementation in medicine "*is based on the wide range and large volume of evidence supporting the health benefits of daily habits and actions*" [18]. The working group with and around Rippe concluded that many adult diseases can already be found in childhood or the daily routine habits of children. The same conditions and types of lifestyle classification are applicable for both treatment and prevention for adults as well as children [18]. The relationship between a healthy lifestyle and bone health has been widely discussed and many findings offer examples of positive and negative influencing factors on bone health being strongly related to a healthy lifestyle, especially considering the consequences of negative lifestyle habits for osteoporosis [19]. Lifestyle-related risk factors such as physical inactivity, low BMI and impaired functional mobility as well as coffee consumption and arterial hypertension have been related to a higher incidence of hip fractures [8]. An inactive lifestyle like increased sedentary behavior and physical inactivity leads to osteoarthritis conservatively treated by total hip arthroplasty [20]. Positive habits on lifestyle have the power to reduce metabolic diseases and the notable influence to reduce morbidity and mortality rates [21]. In search for lifestyle factors, that contribute to cardiovascular diseases, to some types of cancer, to mental illnesses e.g. neuroses as well as digestive and metabolic disorders, nutrition, smoking, alcohol consumption, exercise training, physical activity and obesity were found as parameters with a meaningful role [22, 23]. Key et al. have documented factors related to cancer that are triggered by lifestyle aspects such as obesity and alcohol [24]. Another insight was provided in the study by Parekh and colleagues describing ten small steps of minimal interventions with the potential for promoting healthy lifestyle behaviors [25]. Habits of a healthy lifestyle and the result of a reduced cardiovascular event have been investigated in several observational studies [26–28]. Positive lifestyle behaviors strengthen the assumption of a strong reduction in risk of chronic diseases being evaluated in a large-scale study in the US [29]. Lifestyle is able to operate with influencing factors being discussed along with a further relationship with cardiovascular response as a special way of life connected with body composition and state of health. There are several key modalities to reduce chronic disease that are worth being implemented in daily routine to improve the quality of life and make lifestyle changes [15]. The relationship between cardiovascular and hip related diseases and the treatment of physical activity was presented in the new key findings from the 2018 Physical Activity Guidelines Scientific Report, emphasizing the factors of early childhood, older adults, sedentary behavior, hypertension, type 2 diabetes, body weight/adiposity, brain health and physical activity promotion as being aligned to reduce cardiovascular disease, obesity, stroke, types of cancer, chronic diseases like type 2 diabetes, multiple sclerosis, Parkinson disease and osteoarthritis [30]. These guidelines recommended implementing aerobic activity and muscle-strengthening activities besides balance training in the daily routine as a benefit for better aging. From early childhood through adolescence and up to older age, physical activity offers major health benefits for aging, and especially in older adults this benefit results as a possibility for better aging with a lower risk of injuries, mostly from falls [31]. Sedentary behavior in this context draws a direct relationship of all-cause and cardiovascular disease mortality, the incidence of endometrial, colon and lung cancer and "*mortality risk increases in a dose-response manner with increasing amounts of sitting time; however, this sedentary-related mortality risk is attenuated with greater volumes of moderate-to-vigorous physical activity*" [32]. The connexity of physical activity and hypertension and weight/adiposity behaves similarly, as well as type 2 diabetes, by having an positive impact especially when implementing aerobic training for prevention and treatment [33, 34]. The 2018 Scientific Report called for strategies to overcome the gap between the findings from laboratories and real-life conditions in the population, being faced with the challenge to incorporate researchers' work for public health [30]. Strong evidence is provided by regular physical activity for brain health, cognition, reduction in anxiety and depression as well as amelioration of stress [35]. The overwhelming benefits of regularly physical activity implemented in daily life routines contribute powerfully to improved quality of life. Lifestyle diseases are often influenced by overweight and obesity. In the western world, this reflects a significant health problem due to chronic diseases like cardiovascular diseases, diabetes, cancer, muscular skeletal disorders, arthritis and many others [36, 37]. Possible opportunities to escape this burden include preventing weight gain, reducing energy intake, achieving weight loss, implementing physical activity in one's daily routine and adapting a better lifestyle, improved by more balanced nutrition [15]. Chronic diseases like heart disease, stroke, diabetes, cancer and others are strongly influenced by smoking and drinking alcohol. Evidence has shown the substantial benefit of stopping such bad habits and presenting a risk reduction after a very brief period [38]. A healthy lifestyle promoting a psychological sense of well-being and fewer mental problems is the requirement to prevent mental disorders [39]. The influence and relevance of mental health, emotional well-being and psychological fitness improves the quality of life and achieves a positive effect in lifestyle for the aging population as well as for elderly patients after hip fracture [40, 41].

1.2 Anthropometry and lifestyle parameters in relation with hip operation

Anthropometry is a useful tool to systematically measure the body, involving size, height, weight, structure, measurements of calf circumference (CC), BMI and other components, being possibly predictive as physiological parameters to detect diseases [42]. Anthropometry is an important measurement of the human body that is simple, non-invasive, effective, quick, cost-efficient and quantitatively combinable with valuable assessments of nutritional status [43]. The World Health Organization (WHO) was convened "*to reevaluate the use and interpretation of anthropometric measurements in subject of all ages and to identify reference data for anthropometric indicators*" [44]. This method is available to ascertain the size, proportions and composition of the human body, reflecting a useful choice for selecting and monitoring people for health and nutrition as well as predicting their health and survival. The WHO highlights the relevance of anthropometric measurements, such as height, weight and BMI as an under-used tool for guiding public health policy and clinical decisions and assessing risk of diseases [45]. Body anthropometry is an important and independent factor in defining hip fracture dynamics and fracture prediction related to osteoporosis [46]. In literature, the relation between anthropometric measurements such as height, weight and BMI and hip and knee osteoarthritis has been shown, especially the risk of knee and hip osteoarthritis due to overweight [47]. A low BMI can indicate an increased fracture risk and obesity also shows an association with an increased risk of hip fracture [48]. Positive effects on physical health and longevity as well as mental health are found in marriage [49]. It is established that marital status has an influence on hip fractures, denoting that unmarried people have a higher risk of sustaining a hip fracture, which is in relation to having a different daily life pattern [50]. The influence of marital status on outcomes of total hip arthroplasty has been investigated, whereby it is observed that patients who are unmarried have less clinical benefits after operation and an inferior functional status compared with other patients [51, 52]. The association between education and hip fracture is evident and the grade of education plays a role for hip fractures and osteoarthritis [53]. Fracture risk related with hip operations was higher among people with low education than those with higher educational levels [53]. In patients with a total hip replacement (THA), it was observed that people with university-level education had a 29% risk reduction compared to those who had completed an apprenticeship [52]. A further association with longevity and health as well as lifestyle formative influence is income with an evident relation between higher income and longer life expectancy [54]. Low-income people are less likely to undergo a hip replacement operation compared with high-income people and they are associated with a higher risk of general infection and acute adverse medical events [55]. The relationship between vision and hip fractures due to falls is prevalent in older adults, being linked with associated morbidity [56]. Eye diseases like macular degeneration – diagnosed as an inflammatory disease that progressively increases with advancing age – cause vision loss and visual impairment and present a major burden in the older population [57, 58]. The connection between visual impairment and hip fracture was found in a frail elderly group with poorer vision [59]. Likewise, documented research shows the relationship between hip replacement and eye disease, and especially an increased prevalence of fractures in those with poor vision and macular degeneration, a similar inflammatory process underlying chronic diseases, and the possibility of osteoarthritis [57]. Furthermore, strong connection pain is listed among the many lifestyle parameters to qualify and differentiate patients with hip operation. Due to hip osteoarthritis, people suffer from pain and limitation in physical activity, affected by a lack of function [60]. Pain is associated with muscle weakness, impaired balance and mobility limitations emerging in relation to falls [61]. Total hip arthroplasty is a successful intervention to improve the quality of life in patients with debilitating hip disease, and it is well accepted as a reliable surgery to reduce and eliminate the burden of pain [62–64]. Falls and fear of falling are prevalent risk factors in the older generation and especially fear of falling is a permanent concern of self-imposed limitation in daily activities and a restriction in mobility [65]. Causes of falls are typically multifaceted and can be attributed to muscle weakness, balance deficits, pain, fear of falling and intrinsic or extrinsic risk factors [66].

1.3 FALLS AND FRACTURES

Falls are common causes of injury across all ages, especially in older people, whereby they can result in disability, a loss of independence and mortality. They are an often-overlooked problem, and it has recently been found that there is a connection between falls and geographic factors [67–69]. James et al. have ranked falls as one of the leading causes of reduction in age-standardized rates of disability-adjusted life years, comparable to kidney disease, dementia and asthma [67]. Among adults aged 65 years and older, falls are one of the main reasons of fatal and non-fatal injuries worldwide [68]. For those aged 70 years and older, falls are the leading cause of fatal injury [69]. Approximately one-third of the adults in this age group fall at least once per year, resulting in fractures and other traumatic injuries [70]. A fall is defined as a multicausal event that causes a person to unintentionally find themselves on the ground, floor or other lower level [71–73]. Falls result from the presence of risk factors. A definition of risk factors is given by Rubenstein, who describes them as any characteristic that is found more often in individuals who subsequently experience an adverse event than in those who do not experience this event [74]. In the last two decades, research in fall prevention has found two main categories in connection to falls, namely intrinsic and extrinsic risk factors [75]. Many falls in the age group below 75 years tend to be a result of both factors, including intrinsic factors such as physical activity and extrinsic factors such as a slippery or uneven surfaces, loose cords or mats, poor lighting, and activities associated with a high risk like climbing on a chair to retrieve an object from a high shelf [76]. Intrinsic risk factors tend to primarily influence those in the age group over 80 years, especially including factors relating to disease, injuries, use of multiple medicines, urinary incontinence, stroke and Parkinson disease, reduced cognition, depression and sensory problems such as impaired vision or dizziness, pathology affecting any of the systems involved in balance such as glaucoma – which affects vision – myopathy affecting muscle strength and poor balance and walking ability [77]. In general, the more intrinsic risk factors that are present in a person, the greater the risk of falls [78]. Predisposing risk factors pertaining to all age groups include age-associated changes in strength and balance, age-associated comorbidities such as osteoarthritis, visual impairment, psychotropic medication, and certain footwear [79]. In particular, dementia and falls in older adults are interlinked, and tend to comprise multiple intrinsic and extrinsic risk factors [80, 81]. Figure 1 illustrates as well intrinsic as extrinsic factors and precipitating causes to falling.

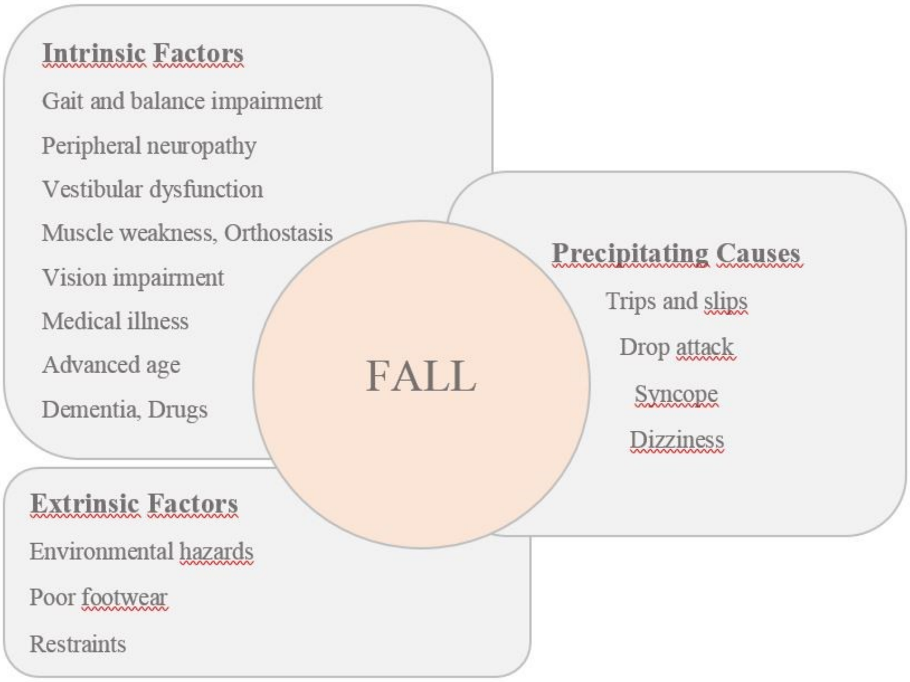


Figure 1: Multifactorial and interacting causes of falls

A central challenge for aging people is avoiding accidents in private homes or community-dwelling residences, with a particular focus on those with osteoporosis or low bone density and osteopenia [82, 83]. Older individuals with dementia need a special focus related to fall prevention like cognitive factors, such as attention or sensory flexibility, psychological factors, such as fear of falling or anxiety, physical and sensory factors like strength or balance, environmental factors like footwear, lighting or walking aids and medical factors like medication side effects and cardiovascular disorders [81]. More than 80% of older adults have at least one chronic condition such as diabetes, the after-effects of a stroke, or arthritis. Further, those in this age group often show increased levels of inactivity, pain and depression, and they commonly take multiple medications, whereby these factors have been related to the prevalence of falls [84]. Past research has also examined the association between cognition and falls. It has been found that they are closely related, and that falls are more prevalent in people with dementia, with the prevalence tending to increase with age [85, 86]. Further, certain fall-related injuries such as hip fractures are associated with mortality within the first six months [87]. Osteoporosis as well as balance problems and cardiovascular disease have also been found to be among the causes of falls [88].

1.4 GRIP STRENGTH

Grip strength (GS) is an accurate and consistent predictor of muscle strength, which – as mentioned above – is a reliable measure related to sarcopenia, as well as mortality and frailty in elderly and middle-aged persons, and it plays a role for biological vitality [89–91]. It reflects the functional status of the upper extremity and has been used in many clinical studies regarding fracture or disease of the upper extremities [92]. Due to its predictive validity, simplicity and portability, GS measurements may be used to screen older adults for further decline [93, 94]. Results of studies show elevated sympathetic nerve activity response to physiological stressors, like GS [95]. Poor hand strength – as measured by GS – has been shown to be a predictor of disability in older people, and a simple and inexpensive screening tool to identify elderly people at risk of disability [96–100]. Further, it has been seen that higher GS is associated with a lower risk of cardiovascular disease and all cancer types [101]. GS can be measured quantitatively by a range of dynamometers, such as hydraulic dynamometers like the Jamar hydraulic dynamometer, electronic dynamometers, pneumatic dynamometers or mechanical dynamometers [102]. A further important point in the measurement of GS is hand dominance. Studies have found that right-dominant subjects were stronger with their right hand, whereas among left-dominant subjects the results were unclear [96]. Of further importance is the position of the person performing the strength test. It has been observed that a supinated position produces the strongest force, whereas a pronated position produces the least amount of force [103]. Further influential aspects include intervals between measurements, the position of the elbow and the shoulder, how the instructions or verbal encouragement are given, and what time of the day the investigation takes place [104–110]. Another remarkable aspect regarding GS is the particular region of the world where the measurement is carried out. A difference between developed and developing regions has been observed, where the results from developing regions have tended to be lower [113]. Research is currently being performed to ascertain standardized cut-off points for GS that can be applied across a range of different countries and regions. GS has the strength to be a prognostic predictor especially in hip fracture patients [111, 112]. Further, GS is an useful indicator for assessing muscle weakness and when the functional results are low it is a significant risk factor for increased length of hospital stay and hospital re-admission [113]. Used in small batteries of measurements, GS is an unavoidable component to set triggers to detect health risks especially in older adults [114]. The GS test is used as a physiological stressor to demonstrate short-term changes of the cardiovascular system [115].

Heart rate (HR) increases during exercise and due to vagal withdrawal in concurrence with the increasing sympathetic activity it is related to poor physical fitness, associated with an impairment of cardiac vagal function during exercise [116].

1.5 Cognitive deterioration

With increasing age, neurological disorders become more prevalent and affect the capacity of the brain regarding the transmission of signals and other neurodegenerative changes, seen in diseases such as Parkinson's or Alzheimer's disease [117]. Speech and language functions appear relatively stable with increasing age [118], although brain size decreases with age, especially in the temporal lobe [119]. The decrease of cognitive abilities leads to a higher risk of falls and slower gait speed, which is also often observed in combination with sedentary behavior [120]. Degenerative dementia is the most common form of late-life cognitive decline, and it is associated with a deterioration of diverse cognitive factors [121]. Evidence has shown connections between a reduced hippocampus volume – associated with memory and cognitive function – and diabetes mellitus, hypertension, obesity, alcoholism and head trauma [122]. A significant association between physical activity and cognitive stimulation has been shown in several studies, suggesting that physical activity has beneficial effects on cognitive function in the elderly population [123, 124]. Outcomes after THA demonstrate a strong association between cognitive impairment and increased post-operative delirium, hospital mortality and complications [125]. Cognitive impairment and dementia have been associated with increased risk of hip fracture due to an increased risk of falls related with mortality and morbidity [126, 127]. Studies have corroborated the relationship between a high risk of hip fractures within two years after the diagnosis of dementia [128].

1.6 The cardiovascular system

Cardiac physiology – meaning the cardiovascular system – is constantly adapting to achieve body homeostasis to maintain the perfusion of tissue with oxygen by adapting diverse aspects of heart activity such as HR, stroke volume, diastole and systole, preload and afterload, which are further elaborated in the following [129]. Diastole refers to the relaxation and filling of the ventricles with blood, and systole refers to the phase of contraction of the ventricles and ejection of blood. Preload relates to volume, as the heart is most filled at the end of diastole, and afterload relates to the pressure that the left ventricle must overcome to eject blood into the aorta during systole. Blood pressure measured within large arteries in the systemic circulation is split into systolic and diastolic blood pressure. Systolic pressure mirrors the maximum pressure within the large arteries when the heart contracts to eject blood through the body, and diastole pressure shows the lowest pressure of the heart in relaxation [130]. Arterial pressure is directly in contact with cardiac output, arterial elasticity and peripheral vascular resistance and can easily be affected by activities. Clinical significance of the arterial pressure regulation is to maintain …*a high enough pressure that allows for proper perfusion of body tissue and organs; but not so high as to cause bodily harm* [130].

1.6.1 ELECTROPHYSIOLOGY

Cardiac muscle cells are electrically excitable. Specialized cells – the so-called cardiac pacemaker cells – are under automatic control, and they are responsible for HR [131]. The electrical circuit has a distinct pathway and flows from the right atrium down throughout the ventricles, starting at the sinus node with a depolarization, further to the atrioventricular node, to the bundle of His, passing the right and left bundle branches, to the Purkinje fibre system [132, 133]. To measure these electrical activity, sequences and electrical signals are recorded by an electrocardiogram (ECG) for determining and visualizing the variability between the heartbeats. A special and important function of the heart is to react immediately to any influence by changing the frequency of heart rate to preserve homeostasis, which means that the difference between two consecutive heartbeats varies from beat to beat [134, 135]. The heart rate is thus a centrally important regulated variable [136]. This variability is called heart rate variability (HRV) and it is an adaptive quality of a healthy organism. Regarding both psychological and physiological stress, it adjusts through a balanced interplay resulting in modulation of the sinus node activity, the pacemaker centre. HRV is the heart's ability to produce fluctuations in the beat-to-beat interval in response to different situations [137]. HRV is different during an exercise period and an immediate recovery compared with rest periods [138]. It is influenced by both the sympathetic (SNS) and parasympathetic nervous systems (PNS), which are two divisions of the autonomic nervous system (ANS) [139]. These two divisions work antagonistically, regulating parts and functions of the body, whereby the so-called "fight or flight" response is related to the SNS and "rest and digest" response is mediated by the PNS [140]. At rest, the vagus nerve represents the main component of the PNS, causing a reduction of HR. By contrast, external stimuli and challenges like heat, cold, pain, and mental stress trigger the SNS and cause an accelerated HR [141]. Besides the modulation of the sinus node activity mentioned above, humoral factors including the renin-angiotensin system and higher regions of the brain play an important role in these processes [142]. ECG – a non-invasive measurement – continuously records heartbeats and measures the time variations between each heartbeat according to QRS complexes. HRV measurements are particularly suitable for status descriptions of the functioning of the cardiovascular system by elaborating the SNS and the PNS. The parameters of HRV used in this research were generally clustered according to the standards of Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology [137]. High-resolution ECG recordings by PowerLab 8/35 were used in this study and subsequent processing was performed according to international recommendations regarding *linear* HRV parameters including time domain (TD), changing of signals over time and frequency domain (FD), including the frequency of signals in a special range. *Non-linear* HRV parameters are commonly demonstrated in Pointcaré plots [143], but were not considered in this study.

1.6.2 Linear parameters - Time domain

The analysis of the time domain is related to how much variability is observed in the recorded HR data, based on the statistical analysis of HR and the length of time between two heartbeats [134]. Specifically, regarding linear parameters, HRV variables relating to the time domain were generated using the standard deviation of normal-to-normal R-R intervals. The standard deviation (SD) of normal-to-normal intervals (SDNN) – measured in milliseconds (ms) – illustrates the general variability and variation in the duration of HR. Elevated sympathetic activity is related to a decrease in SDNN, whereas a higher parasympathetic influence leads to an increase of SDNN levels [144]. The root mean square of successive heartbeat interval differences (RMSSD) – measured in ms – describes the difference of two consecutive NN intervals. RMSSD relates to the short variations of HR and is mediated by the parasympathetic nervous system [146].

1.6.3 Linear parameters - Frequency domain

With the help of the power spectral density (PSD) and the specified frequency bands, conclusions can be drawn about the components of the ANS and the regulatory behavior. Frequency domain variables have been differentiated into various bands of frequency, which are related to physiological regulation of the ANS establishing three different parameters that have been validated by the Task Force [137]. Very low frequency (VLF) – measured in ms^2 – is observed in long measurements with a duration over 24 hours, with oscillations of <0.04 Hz being associated with slow-acting physiological processes such as thermoregulation, metabolism, circadian rhythm, vasomotor tone and the renin-angiotensin-aldosterone system participating in blood pressure controlling being linked to hypotension events [145, 146]. Low frequency (LF) – measured in ms^2 – is defined by the power of the "low" frequency band 0.04–0.15 Hz, and it is mainly modulated by the influence of the sympathetic nervous system, albeit possibly being influenced by the parasympathetic nervous system [147]. A breathing frequency of lower than nine breaths can probably pose an influence and lead to variation in the LF band [148]. High frequency (HF) – measured in ms^2 – is the power of the "high" frequency band 0.15–0.4 Hz and it is influenced by breathing being mediated by the PNS and considered as a measure of the vagus flow [149]. The ratio of LF/HF provides information on the LF band and the sympathovagal balance or change in activity of the sympathetic system, and it measures the proportion of the SNS and PSN that interacts to control the cardiovascular system [137, 150]. This parameter is often used to measure stress responses, and it relates to stress management at baseline levels [151]. Acute external stressors induce an increase of the sympathetic tone or a decrease of the vagal tone, which influences the sympathetic vagal balance in the SNS, and elevates the LF/HF ratio [135].

1.6.4 Influences on HRV

Physiological factors influence HR and HRV. Diseases like heart diseases, lung diseases, renal diseases and psychiatric diseases result in low HRV. External factors like hot climate, noise and pain reduce HRV by an accelerated sympathetic nervous system. HRV has the impact to reflect a general frailty even also in hip fracture patients being possibly used to identify the need for increased surveillance or prophylactic treatment [152]. Further, it is noted that HRV is influenced by diverse factors. Four main types of factors have emerged: genetics, age, gender and circadian rhythms as non-influenceable physiological factors, weight, alcohol behavior, smoking behavior, activity, physical fitness as influenceable life style factors, heat, noise, medications, night shift work as external factors and sepsis, heart disease, psychiatric disease, lung and renal diseases and metabolic diseases as general diseases [153]. With increasing age, decreases in HRV have been observed [154]. Cardiovascular disease (CVD) represents a major burden for aging patients, and age by itself is a dominating risk factor for this [155]. Breathing is related to HRV as the respiratory sinus arrhythmia (RSA) – depending on volume and frequency – and it relates to different frequency bands [156]. Circadian rhythms influence HRV by increasing during the night, with a peak observed in the second half of the night [157]. Smoking and alcohol show a reduced HF and cardiac vagal regulations are lowered [158, 159].

1.6.5 Research on the predictive ability of HRV

The predictive ability of HRV has been studied in various research questions. Investigations into various cardiovascular diseases have shown reduced HRV as being predictive of instances of sudden death [160]. Reduced SDNN – a parameter that indicates overall HR variability – has been observed in patients with heart attack and heart failure, and it has been identified as being one of the most important predictors of cardiovascular mortality [137]. Screening procedures in patients with cardiovascular risks have yielded results of elevated LF and reduced HF in these patients, as well as a change in the sympathetic balance, and reduced SDNN and RMSSD, specifically in those at-risk patients who have diabetes mellitus [161]. The LF power is a significant and strong predictor of mortality, providing prognostic information that can attest reduced HRV at baseline [162]. Pre-operative measurements of HRV provide predictive evidence of post-operative delirium [163]. In areas of hip surgery, HRV can provide information about complications that arise as a result of the surgery and can help surgeons in making more reasonable clinical decisions, reducing the risk of potential medical controversy [164]. Due to the number of complications associated with hip surgery, a tool has to be found to identify low and high risk groups, whereby HRV can possibly be used to verify for care investigation [165].

1.6.6 Physical stressor and HRV

Various stressors and types of tasks relating to physical activity influence HRV in different ways [166]. Physical activity has a high sympathetic activation of the autonomous nervous system and reveals a lower HRV [167]. Research has shown reduced parasympathetic and elevated sympathetic activity in acute physical performance, although after this activity the balance of the vagus nerve actually increases back to the base-level activity, and sometimes goes further above [168]. Vagal balance – obtained by HRV measurement – is important from a predictive standpoint due to its cardio-protection of the vagus nerve [167]. Further, it has been observed that physical activity in older adults has beneficial effects on HRV [169]. A study from Koopman et al. found a lower HRV with lower GS and a higher risk of mortality, which was not influenced by lifestyle-related cardiovascular risk factors [170]. In sum, there have been a large number of studies relating to cardiovascular responses to physical exercise. Relating to handgrip exercises specifically, studies have reported increased heart rate and blood pressure related to these exercises [171]. An important role is played by the association between hip events, fracture and replacement caused by pain and immobility, and GS and the necessity of a cost-effective and rapid implementation in admission assessments [172, 173]. A GS test used for pre-operative observation in patients identifying special pre- or post-operative needs and the prognostic role at hospital admission is highly beneficial [111, 112]. Low GS being extracted as an incidence of hip fractures shows the need for GS testing as an implementation for risk prediction [174].

1.6.7 Mental stress and HRV

Specifically in relation to the influence of mental stress on HRV, stressors such as reaction tests, intelligence tests, work stress and numeracy tests have been shown to modify HRV [175]. Mental stress tends to result in low parasympathetic activity, being characterized by a decrease in HF and an increase in LF [167]. Taelman et al. found an association between performance in a mental test and a reduction in short-term HRV, as well as increased sympathy vagal balance (LF/HF) [175]. They further mentioned that mental stress tends to increase heart rate and reduce HF and vagal tone. Cardiovascular responses to mental load have been studied using a variety of mental stress tasks [176]. Most studies report an increase in heart rate, SBP and/or DBP, and respiratory frequency, and importantly a decrease in HRV during the performance of tasks [177, 178]. Task difficulty has also been linked to physiological responses, with tasks requiring more mental effort eliciting more pronounced physiological responses [179]. In addition, the synchronization of heart, blood pressure and respiration data can provide a more detailed picture of the effect of mental challenge and provide clearer information on the influence of respiration on the different branches of the autonomic nervous system [180]. The current study further investigates the association between mental stress tests and HRV, whereby here mental stress is induced by a Stroop Colour and Word (SCWD) Test. The SCWD test has been shown in previous research to be associated with a significantly reduced HRV due to the extra effort and attention necessary to manage the tasks and depress automatic procedures [181]. The relation between performance in the SCWD test and gender has been investigated and differences in sympathetic activation of the cardiovascular autonomic response in males have been shown [182]. Further, SCWD test and HRV parameters have also been shown to be sensitive to stress in other studies, as well as being a sensitive indicator of different levels of mental stress [183]. Cognitive impairment and dementia in older people were observed with a high prevalence in hip fractures [184].

1.7 AIMS AND RESEARCH QUESTIONS

Finding solutions to improve the health of the aging population is a major challenge for the current health system. Further, rehabilitation in this age group is often complicated and tedious, and it commonly results in assisted-living in community residences. Many studies have been performed to explore topics like elderly people and lifestyle and HRV, healthy lifestyle and special patient groups and lifestyle such as HRV and body strength. Overall, finding and implementing preventive factors – especially lifestyle factors – may be greatly helpful in this context, leading to more effective management of these issues, as well as an increase in personal responsibility related to lifestyle choices affecting these topics. Hip-operated groups have been subject to a wide range field of scientific research relate to diverse aspects and topics in terms of rehabilitation, surgery, treatment, methods of operation, dietary issues and many others. To my knowledge, this study is the first to analyze the relationship between lifestyle and HRV in hip-operated groups. By means of four research questions, it aims to close the gap in literature by showing the relationships between two hip-operated groups regarding lifestyle and cardiovascular impact in relation to physiological and psychological triggers.

1.7.1 Research questions

This study is conducted as a cross-sectional study comparing participants in two hip surgery groups and a control group in stressful situations by using a GS test and a SCWD cognitive stress test as well as their cardiovascular response recordings via ECG to explore relevant predictor variables that specifically could be useful for minimizing falls and pain. The two groups of patients, HFS and THA, who had undergone hip surgery were selected and evaluated due to the different approaches used in treatment and their generally different respective symptoms. Comparing these distinct types of hip surgeries, health profiles of the respective patient groups may allow a better differentiation and may help to match patients to treatments targeting their individual deficits. HFS patients who have suffered a hip fracture that has multifactorial causes may be presumed to show greater frailty – which is related to a deterioration of quality of life – compared with THA patients. THA patients generally suffer from pain due to bone necrosis, coxarthrosis or hip dysplasia. Further, a distinction is aimed at comparing the operated groups with a non-operated population to make a statement that is easy to implement and simple in method.

Four main questions were taken into account regarding these patient groups and the control group, which will be explained in the following. We hypothesize differences in lifestyle as well as differing cardiovascular results related to the pain patients, THA group, compared to fracture patients, HFS group and the control group, which is defined as a group showing standard values representative for this age group.

Research question I dealt with differences in anthropometric parameters between the three study groups. Research question II assumes group differences in lifestyle parameters and cardiovascular parameters and explored how cardiovascular parameters change over time between the three study groups with the possibility to detect an interaction effect among the groups. Research question III tried to find a relationship between lifestyle parameters and cardiovascular parameters among the study groups, and research question IV was oriented to find group differences considering the cognitive task of the STROOP test with the option to elaborate predictors in addition to lifestyle parameters.

2 Material and Methods

All investigations and testing procedures related to this thesis were conducted at the Department of Orthopedic and Trauma at the Klinikum Graz, Medical University Hospital, Graz. The equipment for data collection involved in this investigation is owned by the Department of Physiology and could be used for research purposes during the period of the study. The measurements took place from October 2016 to June 2017 at the Klinikum Graz in the Orthopedics and Trauma departments. This study was carried out as a prospective and monocentric study.

2.1 Inclusion and exclusion criteria

The subject collectively was supposed to represent three different groups, for which test persons had to be acquired as follows. In order to create suitable groups, inclusion and exclusion criteria were set and are listed below in Table 1. Participation in the study was voluntary. The subjects were informed in detail about the planned course of the study and its purpose and gave their written consent. Data were saved in pseudonymized form.

Table 1: Limiting factors for study participation

INCLUSION	EXCLUSION
♦ Men and women between 60 and 85 years	♦ BMI >35
♦ Sufficient knowledge of German to follow the instruction for the investigation process	♦ Dementia and major cognitive impairment
♦ Post hip OP (fracture or arthroplasty)	♦ Neurodegenerative diseases
♦ Healthy people for the control group	♦ Autoimmunological diseases
♦ Written informed consent	♦ Visual and auditive impairment
♦ Reached criteria of the entrance test “Schneller Uhren Dreier”	♦ Severe organic problems
	♦ Drug and alcohol abuse
	♦ Missing compliance
	♦ Simultaneous participation in different studies

2.2 Setting and participants

In order to find suitable investigation groups, it was necessary to proceed according to the selection criteria mentioned above and assign the suitable test subjects to the respective groups. All suitable persons were allocated to the relevant groups and either included or excluded. Patients were examined post-operatively and divided into patients with fall-related proximal femur fracture or medial femoral neck fracture, forming the HFS group, and patients with THA surgery, forming the THA group. A control group – comprising non-current hip-operated people meeting the entrance criteria – were recruited for this project. Originally, 189 patients and people were asked for participation due to possible entrance criteria, of whom 99 (52.3%) agreed to take part in the study. Among these, 23 had to be excluded due to not meeting the ECG entry requirements regarding pathological reasons, and another five patients were excluded due to incomplete data or not continuing with the study, reflecting a total of 28.3%, see Figure 2. [185]

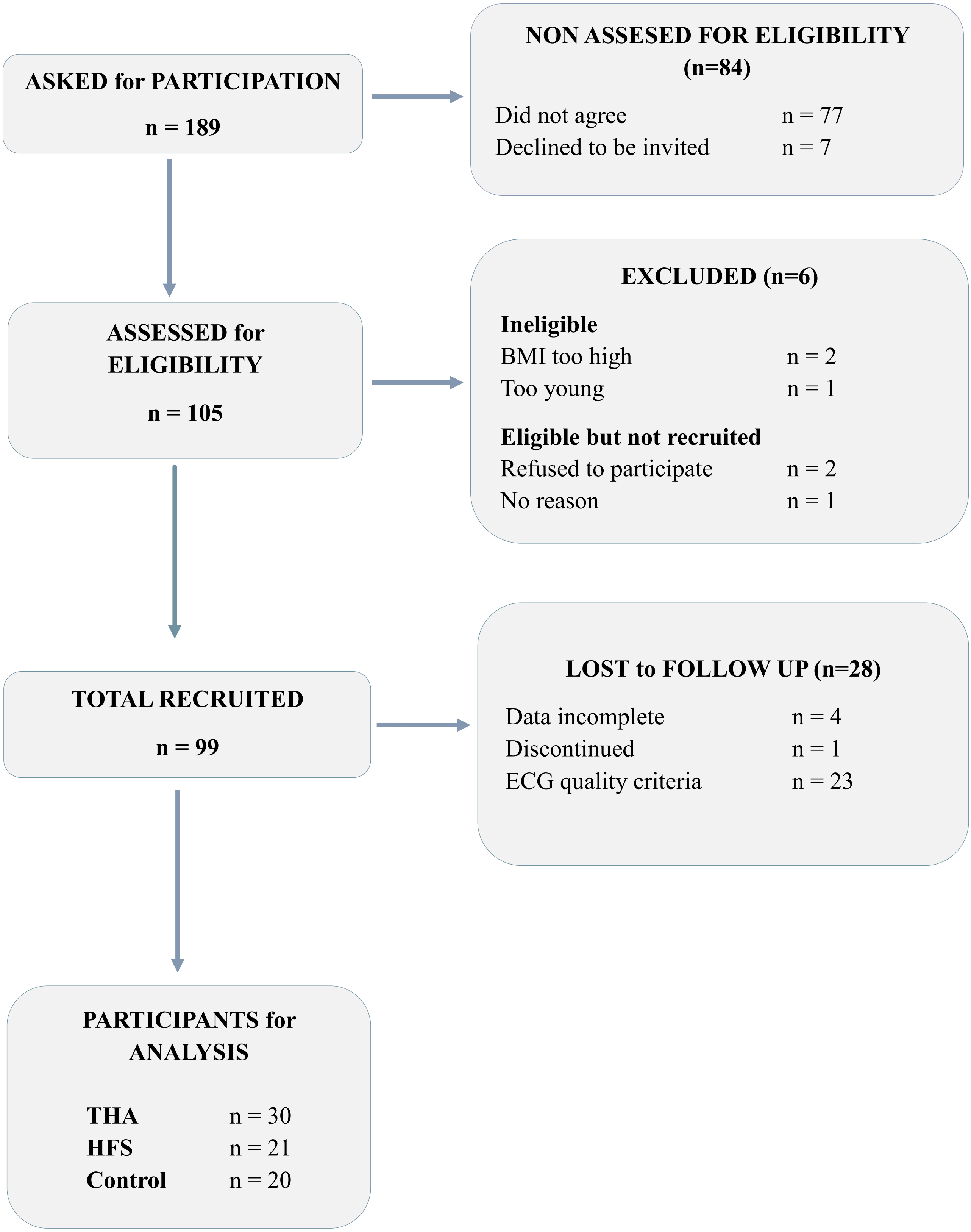


Figure 2: Flowchart. Flow diagram showing the recruitment of participants [185]

2.3 Ethical Approvement

This study was performed according to the convention of the 1964 Declaration of Helsinki and was approved by the national Ethics Committee of the Medical University of Graz (EK-28-515 ex 15/16) [186]. Written informed consent prior to investigation was obtained from all participants after they had received detailed information about the investigation and the study protocol [185].

2.4 Test requirements and components

Anthropometric data of the participants were collected according to the International Society for the Advancement of Kinanthropometry (ISAK) protocol measurements [187]. Measuring weight (participants were asked to remove shoes), a calibrated electronic scale (Seca Modell 799, Germany) was used. Body height was measured to the nearest 0.1cm with an anthropometer (GPM 100, Rudolf Martin Anthropometer, Switzerland) and to collect data of CC a tape measure was used. A testing time between 3 PM and 7 PM was consistent and the same for all participants, following circadian rhythms, and room temperature was always almost the same, at 23°C [137, 188]. For the investigation, it was very important to keep the laboratory quiet by excluding any interrupting noise so that the participants could concentrate well on the experiment to follow the instructions and procedures of the project manager. Participants were requested to abstain from alcohol, caffeine and heavy meals in the two hours prior to testing. After having familiarized participants with the experimental protocol, describing the procedure of the investigation and explaining the singular parts. HR was measured with a limb lead to Einthoven with electrodes being moistened to ensure a good electrical connection and placed at three points of the participant's chest. This bipolar limb derivation by which the Einthoven triangle is formed, mirrored the triangular track whose corners originally represent the two arms and the left leg [189]. In this study, the electrodes were attached to the thorax, which is a common use in clinical practice. A standardized hospital device (Boso Clinicus I, Germany) was used for blood pressure measurements. Further, a breathing belt was placed as tightly as possible horizontally below the large pectoral muscle in male subjects and under the breast line in female subjects. Subsequently, the continuous recording and graphical representation of the HR from transmitter to PC was transferred using the Lab Chart software. A pulse transducer was fixed on the middle finger. During the testing procedure, participants were asked to sit quietly in a constant position without exalted movement to avoid movement artifacts in the heartbeat signal, as seen in Figure 3. Breathing instructions were not given. Data recording was conducted using Power Lab 8/35 of AD Instruments /Australia, PL3508880 exercise physiological system.

Power Lab 8/35 with Lab Chart Pro Software	PL 3508/P
Bio Amp (Amplifier)	FE 132
Disposable ECG Electrodes	MLA1010
Grip Force Transducer	MLT004/ST
Pulse transducer	TN1012/ST
	MLT1132/D
Piezo Respiratory Belt Transducer	

Figure 3: Equipment of investigation. With permission of my father to publish this picture.

2.5 INVESTIGATION PROCEDURE

Elderly individuals often experience an imbalance in autonomic nervous activity due to surgical stress, causing us to start investigation after the third post-surgery day. Testing time was between the third and tenth day after surgery, and circadian rhythms were taken into account [137, 188, 190]. During the entire experimental procedure, patients had to sit quietly in a comfortable chair that was adjusted for each person and asked to avoid speaking or moving abruptly. The study protocol comprised an adaption period followed by a 3 min measurement at rest to record baseline results. Thereafter, participants were instructed to press a GS dynamometer in supine position as strongly as possible for three seconds, twelve times with a twelve-second break after each turn, to produce physical stress. Finally, a further 3 min measurement at rest followed to record recovery results. A cognitive stress test – SCWD test – followed and a final 3 min measurement at rest concluded the investigation. Prior to and after ECG recordings, blood pressure was measured. At the end of the investigation, participants were thanked and given a "Studienschokolade", shown in Figure 4, for participating in the study. [185]

Figure 4: A chocolate as a small present for participation

The following Figure 5 can serve to illustrate the investigation process in detail.

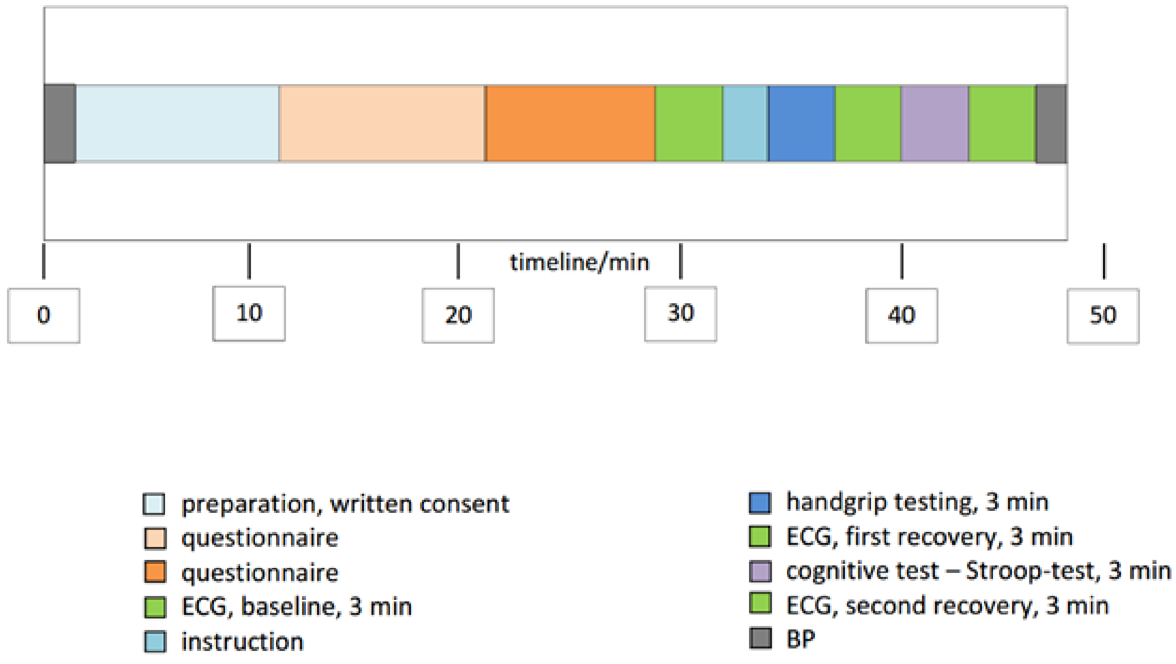


Figure 5: Investigation process and time schedule
The figure above offers a schematic overview of stages of the investigation being performed by the same procedure for each participant.

2.6 Applied Trials

Questionnaire-related parameters like socio-demographic data were asked and documented in connected form by an interview lasting about 20 minutes. The "Schneller Uhren Dreier", was taken as an entrance test to participate in the study, the interference test - SCWD test, provides the contribution to the mental stress test and Barthel - Index survey was chosen as a test for collecting everyday situations, respectively.

2.6.1 "Schneller Uhren Dreier"

The so-called mini-cog test is a questionnaire serving as a dementia exclusion procedure, comprising three short questions covering the areas of orientation, memory and concentration. It is a very easy-to-perform screening, with the patient having to remember three terms that the study leader has told them. Subsequently, it is expected that the patient can draw a clock with all twelve digits and a specified time (11:10 a.m.). The three previously mentioned terms should then be repeated. With a perfect watch test and three remembered words, no suspicion of dementia was confirmed. Slight errors in the watch test and one or two remembered words showed a light form of dementia and serious errors in the watch test and no remembered words demonstrated a severe course of dementia. The test had a sensitivity of 96 percent and a specificity of 72 percent. In the study, this test serves as an entry requirement to create the sample [191, 192].

2.6.2 "Stroop color and word (SCWD) test"

As an objective and reliable, multi-dimensional performance test, the color-word interference test measures elementary skills of information processing (selection, coding and decoding) in the optical-verbal functional area. The test records processing speeds of the "Sensu-Konzepto-Motor" (perception, conceptual implementation and verbal reproduction of stimuli by reading or naming). Using the color-word incongruity principle according to J.R. Stroop also varies the stress load and thus the concentrative load. The cognitive performance functions that can be measured with the test are nomination (speed of naming, naming), selectivity (concentrative resistance to dominant reaction tendencies or tendency to interference), alertness (basic speed of information processing) and – under certain conditions – reading speed. The evaluation provides a three-dimensional performance profile. The color-word interference test was used to quantify the focused attention and willingness to react in the verbal-optical area. This comprises three test panels with color words, color fields and colored color words as test stimuli. The test subjects had to read Panel I with the color words as quickly as possible, then name the color fields of the second panel – Panel II – and finally the colors of the different color words of the third panel, the interference table. The instruction was also standardized according to a given text. Panels I and II contained 36 specifications in landscape format (6x6) such as the word "red", "yellow", "blue" and "green" or color fields in an unsystematic sequence. All twelve possible incongruent combinations of the colors and words mentioned were represented three times on the interference table. In contrast to Panel I and II, a test line was introduced in Panel III to clarify the task as a header. The additional time required in seconds to process the interference table serves as a test value, calculated from the difference in processing time between the second and third tables. Incorrect terms were immediately displayed visually by the test manager and had to be repeated by the test person until they were correct [181, 193–196].

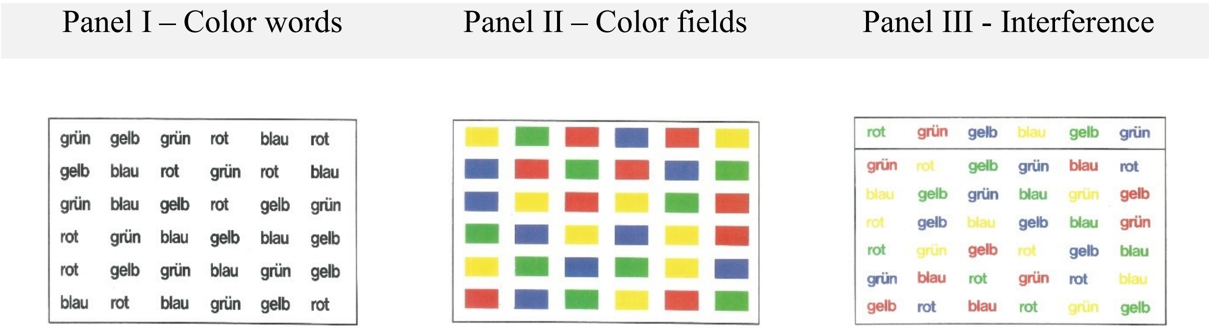


Figure 6: SCWD testing materials, word and color panels

2.6.3 "Barthel Index"

The Barthel Index is used to assess activities in everyday life, dividing everyday activities into ten sub-items. For each area of activity, it must be specified whether the patient can perform this activity alone, with help or not at all. The maximum score is 100, describing a patient who can take care of him-/herself without additional help. It was used in this study as a marker for self-manageable life [197–199].

2.7 Data acquisition and pre-processing

Continuous ECG was recorded using the exercise physiology and software system Power Lab 8/35, with Lab Chart Pro Software all from AD Instruments (Sydney, Australia), with a sampling rate of 1000 Hz. GS – derived from a GS transducer – ECG and respiration frequency – derived from a chest strap – were indicated by three channels on the device. Disposable electrodes were fixed at the thorax (2-lead, 1 channel position), and bipolar limb derivation using an Eindhoven Lead II setup gave the recorded binary data which were saved in European Data Format (EDF) [200]. The R-wave detection was carried out using a revised MATLAB function (MATLAB®, Math Works Natick, Massachusetts, USA) and the immediate beat-to-beat heart rate was also calculated using this function [200]. Artifact handling was performed semi-automatically by a visible check of every signal, in combination with a MATLAB function that identified these signals according to the following criteria: 1) ectopic beats, 2) physiological limits and 3) maximal percentage of change in relationship to standard deviation of the signal. Therefore, we used time series with equidistant time steps, after resampling beat-to-beat values at 4 Hz, using piecewise cubic spline interpolation. Ectopic beats were as well visually controlled as surveyed and single artifacts were replaced by linear interpolation and only time series higher than 85% validity were used for further analysis. [185]

2.8 STATISTICAL ANALYSIS

All statistical analyses used in this work were carried out by the Statistical Packages for the Social Sciences, SPSS, IBM SPSS Statistics Version 26 for Windows (SPSS Inc., Chicago, USA).

All parameters were checked for normal distribution. Age, SBP and DBP as GS and weight, height, BMI, CC, the anthropometric parameters, were chosen for analysis. GS had to be transformed by a z-transformation to be ready for analysis. In this study, the variables HR, SDNN, RMSSD, HF, LF, and LF/HF of the HRV analysis were chosen for analysis. Every continuous variable of the HRV parameters and the GS results as well as the results of the SCWD test and the anthropometric parameters of the data set were checked for normal distribution by the Kolmogorov-Smirnov test and Q-Q-Plot analysis. All variables were within a normal distribution except SDNN, RMSSD, LF and HF, which had to be transformed by a natural logarithm (*ln*) for further analyses. The following lifestyle parameters were chosen, dichotomized and set available for statistical analyses: marital status ranged between married or in a relationship, coded as 1 and single, coded as 0; education ranged between high-school education, coded as 1 and no educational qualification, compulsory school or apprenticeship, coded as 0; income ranged between >1,400 €, coded as 1 and an income lower than 1,400 €, coded as 0; smoking and alcohol consumption, fracture, osteoporosis, eye disease, pain, falls, fear of falls were coded dichotomously as yes = 0 and no = 1, kinetic behavior, sports kid and activity were coded dichotomously as yes = 1 and no = 0; health status was termed as good, coded as 1 or bad, coded as 0; sedentary behavior was termed being active (physical activity), coded as 1 or a sitting lifestyle, coded as 0; sitting time was indicated by 1-3 hours per day, coded as 1 and >3 hours, coded as 0 and a Barthel Index above 80 points, coded as 1 and 0-80 points, coded as 0.

The level of significance was set to 5% and the alternative hypothesis could be accepted if $p < .05$. Descriptive statistics are presented as mean ±, for the central tendency of continuous data and SD to observe the variability of continuous variables. Absolute and relative frequencies are used to show the distribution of nominally or ordinally scaled variables. Differences in anthropometric parameters, lifestyle parameters and HRV parameters between the three study groups were performed by the analysis of variance, ANOVA.

Regarding research question II, the HRV parameters were analyzed for significant differences over time using the ANOVA with repeated measures. This analysis was used to find changes of physiological variables over time and investigated the effects for the different groups. The variables were checked for homogeneity of variance by the Levene test, and for sphericity by the Mauchly test. Corrections were carried out for sphericity violations according to the Greenhouse-Geisser correction. Post-hoc tests with Bonferroni pairwise comparison were carried out to find differences among the groups.

The extent to which cardiovascular parameters change in relation to a stressor – here the GS test – was compared to the levels at rest. This was examined using an ANOVA with repeated measures. The measurement repetition factor was the time of measurement with three levels: first, the baseline, three minutes at rest before the GS phase, then the GS phase, and third the recovery, three minutes at rest immediately after the GS phase. Cardiovascular parameters were recorded as dependent variables. Partial eta squared, η^2, was used as the default effect size measure and values η^2=.01 can be interpreted as a small effect, $\eta^{2=}$.06 as a medium effect and values $\eta^2 \geq .14$ as a large effect [201].

In the context of research question III, correlations between HRV and lifestyle parameters were applied by a linear correlation according to Pearson. The coefficient r was used to investigate correlations between cardiovascular parameters and lifestyle factors. For interpretation, <0.3 represents a small effect, 0.3-0.5 a medium effect and ≥0.5 a strong effect [202].

Regarding research question IV to find predictors for SCWD test, the logistic regression was chosen as an appropriate analysis. The assumptions for regression analysis were checked by the Durbin Watson test for statistical independence, Q-Q plots for normality, scatter plot of residuals vs predicted values for checking linearity and homoscedasticity and variance inflation factors were employed for checking multicollinearity. The values range from 0 to 1, with 0 being a poor model and 1 being a perfect model.

3 RESULTS

The results of this study are presented in the following sections by describing and analyzing parameters to all research questions associated with the comparison of the study groups pertaining to all relevant parameters.

3.1 ANTHROPOMETRIC PARAMETERS

One of the aims of this study was to analyze anthropometric and other parameters including age, height, weight, BMI, CC, SBP, DBP and GS between the three study groups. Age did not significantly differ between the groups. The mean age of the THA group was 71±6.7 years, for the HFS group it was 74±5.5 years and for the control group 71±6.7 years. ANOVA results of the following parameters showed significant differences between the three groups: BMI p=.002, weight p=.003, CC p=.012, SBP p=.038 and DBP p=.026, shown in Figure 7. The full results are shown below in Table 2.

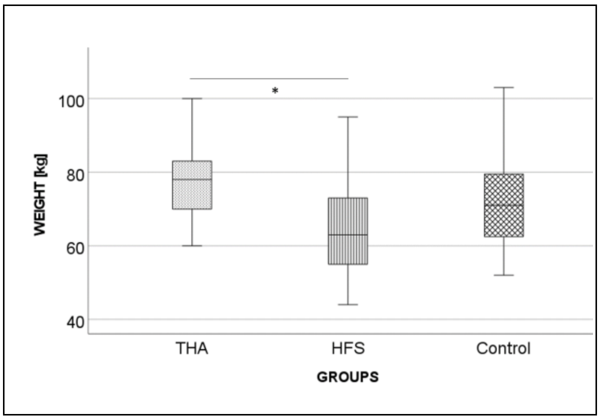
Table 2: Characteristics of the study groups

Table 2 shows significant results by highlighting and marking. Data of the study groups are shown as means (±SD) and minimum and maximum values of age [y], height [cm], weight [kg], BMI [kg/m²], CC [cm], SBP [mmHg], DBP [mmHg], GS [N] and GS z-transformed by gender.

	THA n=30	HFS n=21	Control n=20	TOTAL n=71	Analysis of variance p-value*
Female/male (n)	(13/17)	(15/6)	(12/8)	(40/31)	
	mean (±SD) min/max	mean (±SD) min/max	mean (±SD) min/max	mean (±SD) min/max	
Age [y]	71 (± 6.71) 61/85	74 (± 5.5) 62/84	71 (± 6.72) 60/83	71 (± 6.51) 60/85	F(2,68)=2.335 .105
Height [cm]	170.5 (± 8.95) 151/187	167.2 (± 9.10) 154/180	169.4 (± 8.40) 158/187	169.2(± 6.8) 151/188	F(2,68)=0.748 .477
Weight, [kg]	76.9 (± 9.72) 60/100	65.1 (± 12.52) 44/95	72.7 (± 13.36) 52/103	72.2 (± 12.5) 44/103	F(2,68)=6.391 **.003***
BMI [kg/m²]	26.5 (± 2.84) 21/33	23.1 (± 3.64) 17/33	25.2 (± 3.23) 21/34	25.1 (± 3.46) 17/34	F(2,68)=6.773 **.002***
CC[cm]	35.6 (± 3.60) 29/43	33.9 (± 3.30) 29/41	37.1 (± 2.37) 31/41	35.5 (± 3.38) 31/41	F(2,68)=4.769 **.012***
SBP [mmHg]	132 (± 13.0) 105/160	123 (± 10.01 100/140	129 (± 11.16) 99/145	128.32 (± 12.1) 99/160	F(2,68)=3.418 **.038***
DBP [mmHg]	76 (± 8.36) 55/90	71 (± 7.82) 55/80	77 (± 7.61) 65/90	74 (± 8.17) 55/90	F(2,68)=3.832 **.026***
GS [N]	198.1 (± 70.3) 82.4/306.8	152.4(± 103.3) 38.4/438.5	213.5 (± 78.4) 90.4/345.9	187.94 (± 88.4) 47.3/458.1	F(2,68)=4.025 **.022***
GS z-transformed by gender	-0.04 (± 0.856) -1.97/1.34	-0.31 (± 1.191) -1.55/-0.31	0.38 (± 0.869) -1.81/1.87	0.0 (± 1.0) -1.62/3.12	F(2,68)=2.467 .080

Post-hoc comparisons showed significant differences between the HFS group and the other groups: weight, p=.002, BMI, p=.001 and SBP, p=.034 were significantly lower in the HFS group than the in THA group, and CC, p=.009 and DBP, p=.048 were significantly lower in the HFS group than in the control group.

1



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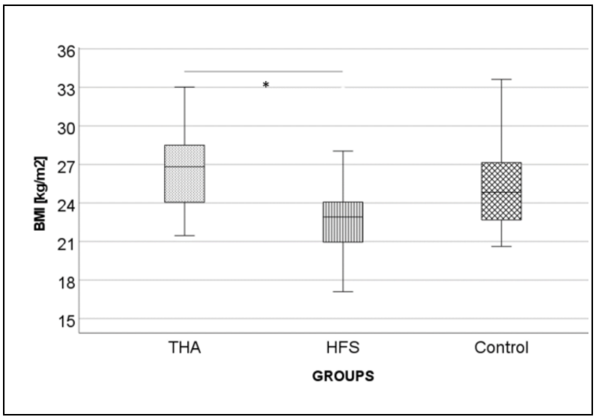

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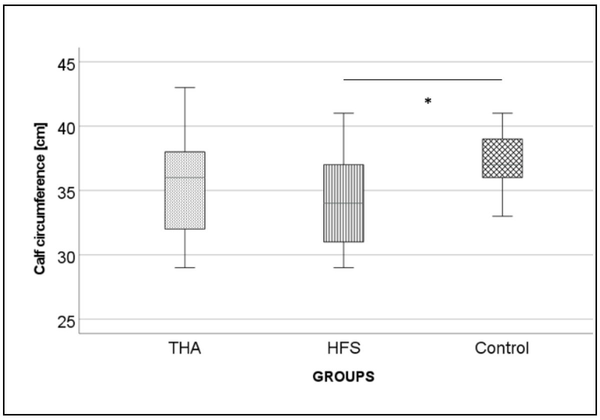

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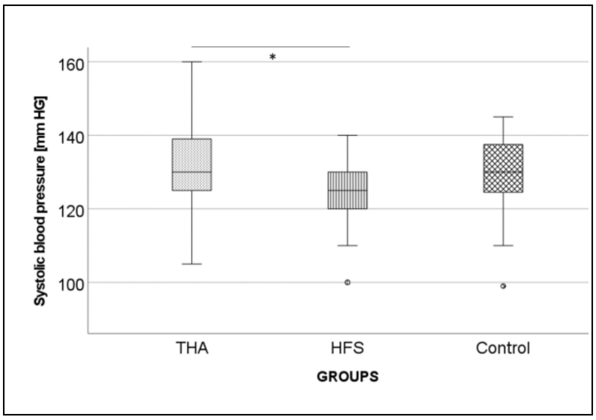

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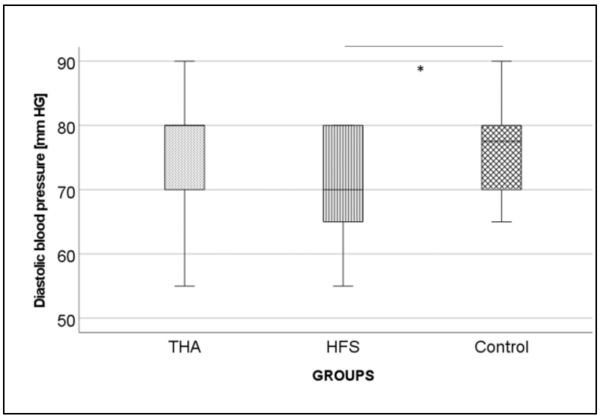


Figure 7: Significant group differences in weight (1), BMI (2), calf circumference (3), SBP (4) and DBP (5)

3.2 Analysis of Lifestyle parameters among the groups

The results of the second research question provide insights into lifestyle and cardiovascular activity among the three study groups with the aim to possibly maintain different characteristics among the groups.

Lifestyle parameters were analyzed in all groups using ANOVA and the results are presented in the Table 3. The listed parameters could be considered significant and were made visible by highlighting. These are education, income, smoking, fracture, eye disease, kinetic behavior, pain, activity, falls and fear of falls.

Table 3: ANOVA results of lifestyle parameters between the groups

	F/df	p value	Post-hoc test	
Marital status	2.457 (2,68)	.093		
Education	3.989 (2,68)	**.023**	THA/control	p= .021
Income	3.750 (2,68)	**.029**	HFS/control	p= .030
Smoking	7.140 (2,68)	**.002**	HFS/control	p= .001
Alcohol	.286 (2,68)	.752		
Fracture	16.719 (2,68)	**<.001**	THA/HFS THA/control HFS/control	p= <.001 p= .026 p= .022
Osteoporosis	1.173 (2,68)	.316		
Eye disease	6.434 (2,68)	**.003**	HFS/control,	p= .002
Kinetic behavior	13.730 (2,68)	**<.001**	THA/control HFS/control,	p= <.001 p= .015
Health status	2.129 (2,68)	.127		
Pain	32.111 (2,68)	**<.001**	THA/control HFS/control	p= <.001 p= <.001
Sports kid	1.598 (2,68)	.210		
Physical activity	8.043 (2,68)	**.001**	THA/HFS, HFS/control	p= .001 p= .039
Falls	74.019 (2,68)	**<.001**	THA/HFS HFS/control	p= <.001 p= <.001
Fear of falls	4.718 (2,68)	**.012**	HFS/control	p= .011
Sedentary behavior	2.274 (2,68)	.111		

Sitting time	.993 (2,68)	.376
Barthel Index	.677 (2,68)	.512

Post-hoc tests offer clues about group connections in diverse parameters. Significant differences were seen in education, whereby the THA group had a significantly lower education than the control group, income was significantly lower in the HFS group than in the control group, smoking was significantly higher in the HFS group than in the control group, fracture was significantly lower in the THA group than in the HFS group, significantly higher in the THA group than in the control group and significantly higher in the HFS group than in the control group, eye disease was significantly higher in the HFS group than in the control group, kinetic behavior was significantly lower in the THA group than in the control group and significantly lower in the HFS group than in the control group, pain was significantly higher in the THA and HFS groups than in the control group, physical activity was significantly higher in the THA group compared to the HFS group and significantly lower in the HFS group than in the control group, falls were significantly higher in the HFS group than in the THA group and significantly higher in the HFS group than in the control group and fear of falls was significantly higher in the HFS group than in the control group.

3.3 Group differences in HRV parameters

To get approaches for a differentiation among the study groups, this investigation for HRV parameter evaluation is divided into three subgroups as follows. Beginning with the examination of the baseline differences, further the differences in the parameters over time and finally the interaction effect between time and group; these analyses are intended to shed light on possible differences between the groups.

3.3.1 Baseline differences of the study groups

In the following part, HRV parameters of baseline data were shown for each group separately. HR parameters had the numerically highest values in HFS (82.49±12.45) followed by THA (78.14±10.76) and lowest values in the control group (71.42±11.64), *ln*SDNN showed the highest values in the control group (3.02 ±.55) followed by the THA group (2.80±.53) and with lowest values in the HFS group (2.59±.42). *ln*RMSSD had highest values in the control group

(2.59±.79) followed by the THA group (2.32±.73) and had the lowest values in the HFS group (2.10±.73). The *ln*LF parameter demonstrated the highest values in the control group (1.47±.25) followed by the THA group (1.33±.34) and the lowest values in the HFS group (1.16±.33). The *ln*HF parameter had the highest values in the control group (1.27±.46) followed by the THA group (1.13±.39) and the lowest values in the HFS group (.86±.66). The ratio of LF/HF had the highest values in THA group (.66±1.12) followed by the control group (.59±.92) and the lowest values in the HFS group (.57±.96). There were only significant baseline differences between the HFS group and the control group namely in HR, *ln*SDNN, *ln*LF and *ln*HF. No significant differences at baseline were observed in the parameters *ln*RMSSD and LF/HF. All HRV baseline values of the descriptive statistics and ANOVA results are presented in Tables 4 and 5, respectively.

Table 4 Descriptive statistics of baseline values of HRV parameters for the THA, HFS and control groups

THA Group	HR bpm mean (±SD)	*ln*SDNN ms mean (±SD)	*ln*RMSSD ms mean (±SD)	*ln*LF ms^2 mean (±SD)	*ln*HF ms^2 mean (±SD)	LF/HF (-) mean (±SD)
Baseline	78.14 (±10.76)	2.90 (± .53)	2.32 (±.73)	1.33 (±.34)	1.13 (±.39)	.66 (±1.12)
HFS Group	HR bpm mean (±SD)	*ln*SDNN ms mean (±SD)	*ln*RMSSD ms mean (±SD)	*ln*LF ms^2 mean (±SD)	*ln*HF ms^2 mean (±SD)	LF/HF (-) mean (±SD)
Baseline	82.49 (±12.45)	2.59 (± 0.42)	2.10 (±.73)	1.16 (±.33)	.86 (±.66)	.57 (±.96)
Control Group	HR bpm mean (±SD)	*ln*SDNN ms mean (±SD)	*ln*RMSSD ms mean (±SD)	*ln*LF ms^2 mean (±SD)	*ln*HF ms^2 mean (±SD)	LF/HF (-) mean (±SD)
Baseline	71.42 (±11.64)	3.02 (±.55)	2.59 (±.79)	1.47 (±.25)	1.27 (±.46)	.59 (±.92)

ANOVA results of baseline HRV parameters showed significant values in HR, *ln*SDNN, *ln*LF and *ln*HF, as shown in Table 5.

Table 5: ANOVA results of baseline HRV parameters

	df	F	p	Post-hoc test HFS/Control
HR	2.68	4.80	**.011**	**.009**
*ln*SDNN	2.68	3.67	**.031**	**.026**
*ln*RMSSD	2.68	2.29	.109	
*ln*LF	2.68	4.89	**.010**	**.008**
*ln*HF	2.68	3.58	**.033**	**.032**
LF/HF	2.68	0.57	.945	

3.3.2 Changes of parameters over time

ANOVA results revealed a main effect of time and an interaction effect for time*group, listed below in Table 6.

Table 6: Repeated measures ANOVA results of the three study groups

	Main effect **time**			Interaction effect **time*group**			Post-hoc tests	
	F (df)	p	η^2	F (df)	p	η^2		
HR	66.46 (1.29, 87.85)	**<.001**	.494	2.50 (2.58,87.85)	.073	.069	HFS/C **.009**	THA/C .078
*ln*SDNN	41.63 (2,1,36)	<.001	.380	3.16 (4, 14)	**.016**	.085	HFS/C **.004**	
*ln*RMSSD	10.41 (2, 14)	**<.001**	.133	1.674 (4, 14)	.160	.047	-	
*ln*LF	66.76 (2,14)	<.001	.495	1.96 (4,14)	.104	.055	**-**	
*ln*HF	.72 (2,14)	.488	.010	1.21 (4,14)	.308	.034	**-**	
LF/HF	62.72 (1.67,113.60)	<.001	.480	2.05 (3.34,113.60)	.104	.057	**-**	

Significant ANOVA data analysis results of the main effect of time were observed in HR, *ln*SDNN, *ln*RMSSD, *ln*LF and LF/HF. *ln*HF demonstrated no significant results.

In the following presentation a detailed analysis of the main effect of time is showed referring to differences of the various stages of the investigation: baseline, GS and recovery.

HR significantly increased from the baseline, 77.53±12.13 to GS 81.73±12.81, p<.001 and significantly decreased from GS to recovery, 77.95±12.54, p=<.001. Baseline and recovery did not significantly differ from each other, p=.481.

*ln*SDNN significantly increased from the baseline, 2.80±.52 to GS 3.13±.57, p=<.001 and decreased significantly from GS to recovery, 3.02±.48, p=.001. Baseline and recovery significantly differed from each other, p=<.001.

*ln*RMSSD significantly increased from the baseline, 2.33±.74 to GS 2.34±.72, p=<.001 and significantly decreased from GS to recovery, 2.37±.74, p=.004. Baseline and recovery did not significantly differ from each other, p=1.000.

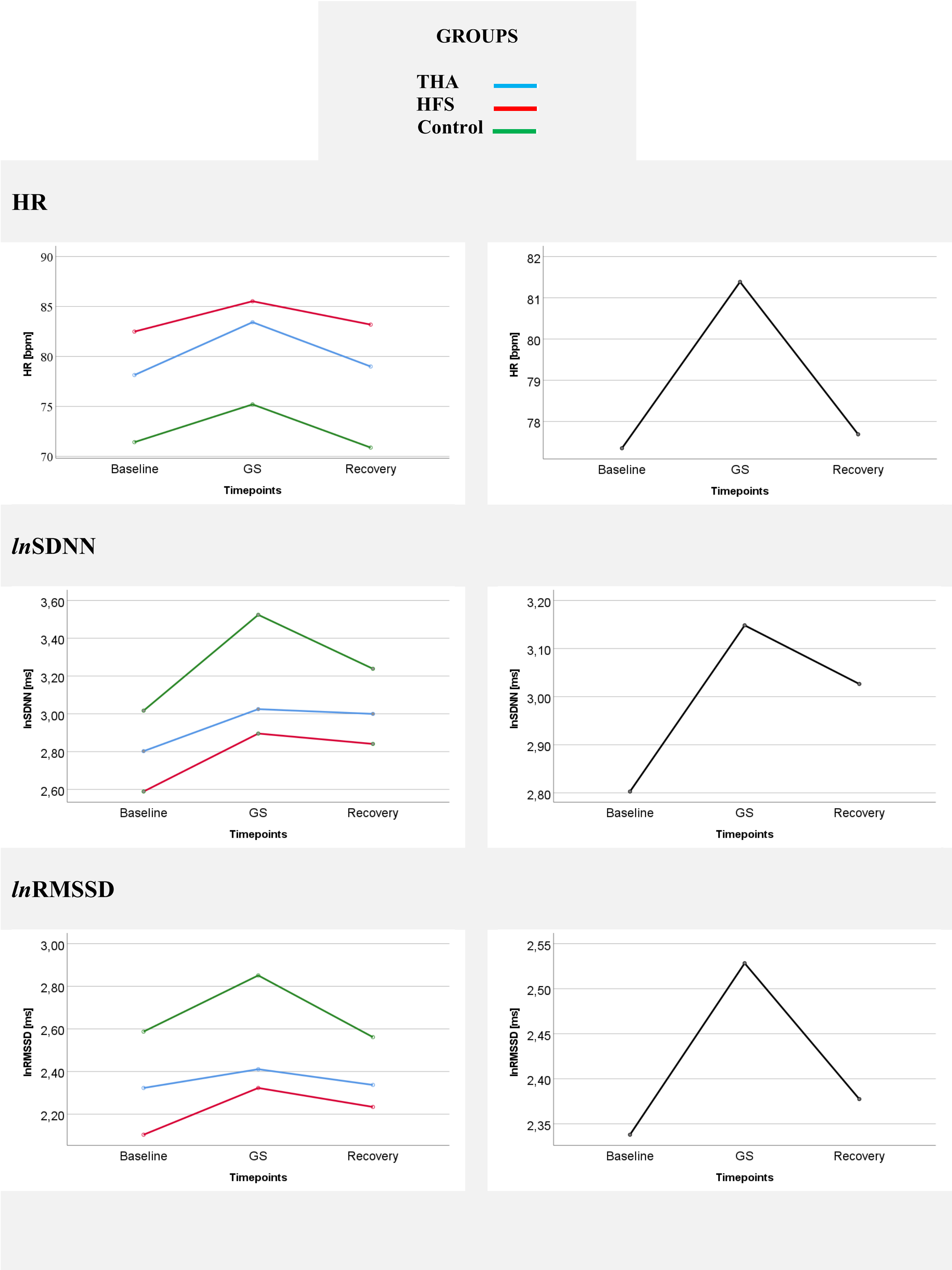
*ln*LF significantly increased from the baseline, 1.32±.33 to GS 1.62±.30, p=<.001 and significantly decreased from GS to recovery, 2.37±.74, p=.001. Baseline and recovery significantly differed from each other, p=.006.

*ln*HF did not significantly increase from the baseline, 1.10±.52 to GS 1.12±.58, p=1.000 and did not significantly decrease from GS to recovery, 1.08±.56, p=.942. Baseline and recovery did not significantly differ from each other, p=1.000.

LF/HF significantly increased from the baseline, .61±1.01 to GS 1.77±1.05, p=<.001 and it decreased significantly from GS to recovery, .88±.99, p=<.001. Baseline and recovery significantly differed from each other, p=.005, seen in Figure 8.

3.3.3 Interaction effect between time and group

The analysis of the interaction effect of time*group revealed significant results in the *ln*SDNN parameter. Significant differences of post-hoc tests were observed between the HFS group and the control group, p=.004. In addition, a trend towards significance was observed in HR, p=.073, also supported by significant differences in post-hoc tests between the HFS group and the control group p=.009 and nearly significant outcomes between the THA group and the control group p=.078. These results are illustrated in Figure 8.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HR [bpm]
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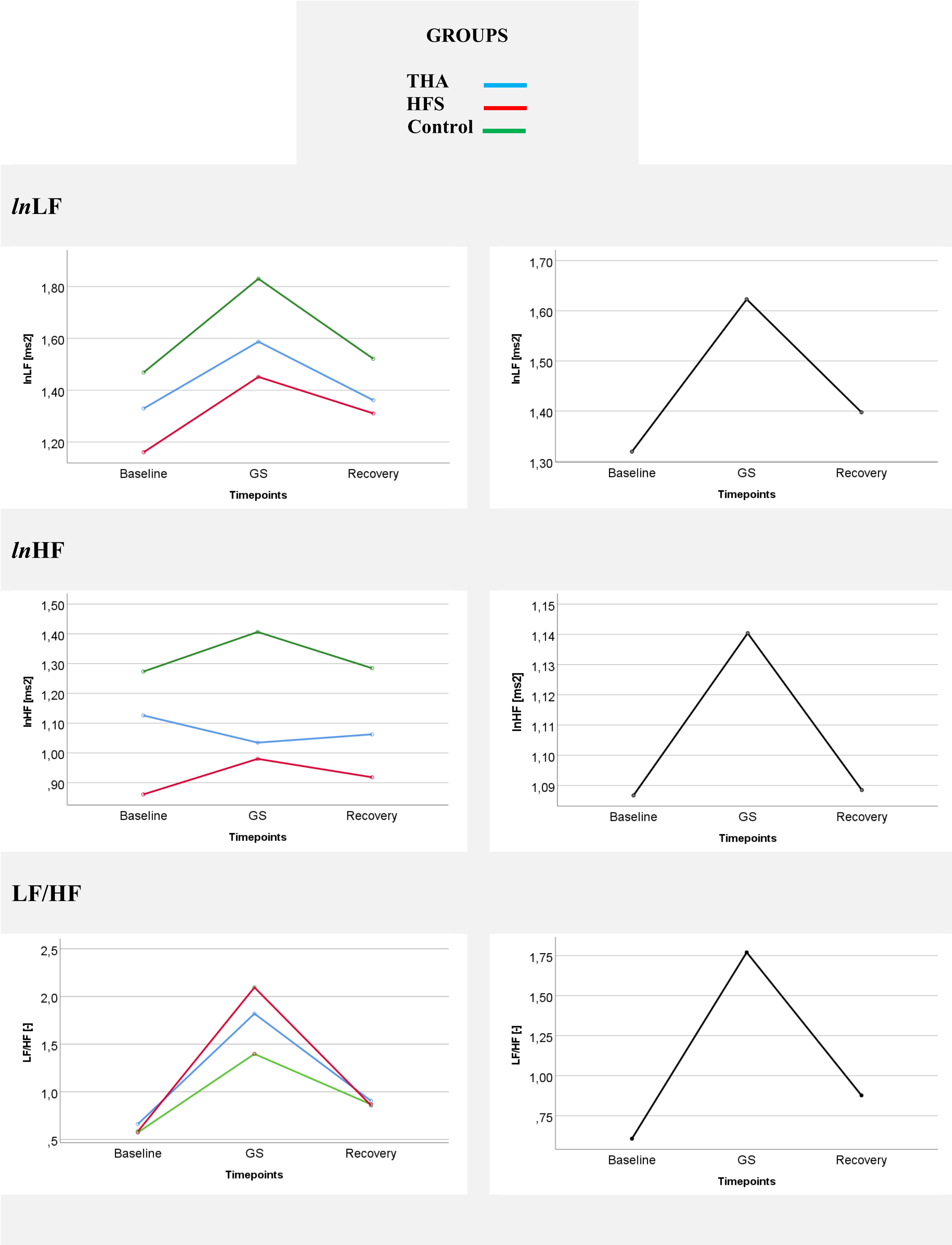

Figure 8: HRV parameters over different stages of investigation
The right figures show means across the pooled main effect time of the groups, the marginal means, and the left figures show the study groups individually across the different stages of investigation.

3.4 Relationship between lifestyle and cardiovascular parameters

Following the third research question, given below results could be found by using the correlation analysis between HRV baseline parameters and lifestyle parameters. Weak to moderate correlations revealed in several parameters, see Table 7. All significant results are highlighted in light gray and marked by an asterisk.

The influence of lifestyle parameters on HRV parameters is described in the following part and illustrated in Figure 9.

HR showed a weak positive correlation with kinetic behavior, r=.256, p=.031, health status, r=.236, p=.048 and falls, r=.298, p=.012. Correlation analysis showed the higher the HR baseline values of a proband were, the lower was the personal feeling about one's health status, the higher was the tendency to fall and the more limited was the kinetic behavior.

A weak positive correlation has been observed between education and *ln*SDNN, r=.241, p=.043, a weak negative correlation between falls and *ln*SDNN, r=-.291, p=.014, and a weak positive correlation between sedentary behavior and *ln*SDNN, r=.235, p=.048. Lower values in *ln*SDNN baseline showed a trend towards more sitting and enhanced falling. Higher *ln*SDNN baseline values were seen in people with higher education.

*ln*LF showed a weak negative correlation with age, r=-.274, p=.021 and falls, r=-.293, p=.013, whereas a weak positive correlation was seen with education, r=.263, p=.027. Higher *ln*LF baseline was expressed in higher education values and a lower tendency to fall. With increasing age, *ln*LF baseline declined.

*ln*HF further showed a weak negative correlation with falls, r=-.242, p=.042. Higher *ln*HF baseline presented a lower tendency to fall.

No correlation has been observed between *ln*RMSSD and the ratio of LF and HF and the lifestyle parameters.

Table 7: Results of correlation analysis between HRV parameters and lifestyle parameters

	Age	BMI	CC	Education	Income	Smoking	Alcohol	Eye Disease	Kinetic Behavior	Health Status	Pain	Sports Kid	Activity	Falls	Fear of falls	Sedentary behavior	Sitting time
HR r=	0.037	-0.016	-0.022	-0.175	-0.107	0.087	-0.056	0.229	.256*	.236*	0.111	-0.127	-0.073	.298*	0.011	-0.234	-0.016
*ln*SDNN r=	-0.142	0.054	0.147	.241*	0.141	-0.072	0.015	-0.190	-0.184	-0.211	-0.111	0.211	0.086	-.291*	-0.110	.235*	0.149
*ln*RMSSD r=	-0.059	0.079	0.169	0.152	0.075	-0.004	0.010	-0.019	-0.091	-0.093	-0.067	0.042	-0.052	-0.229	-0.064	0.197	0.135
*ln*LF r=	-.274*	-0.020	0.000	.263*	0.115	-0.062	0.068	-0.208	-0.232	-0.084	-0.101	0.223	0.085	-.293*	-0.131	0.133	-0.001
*ln*HF r=	-0.117	0.061	0.099	0.115	0.054	-0.100	0.000	-0.064	0.001	-0.007	-0.011	0.047	-0.142	-.242*	-0.014	0.131	-0.016
LF/HF r=	-0.183	-0.054	-0.127	0.094	0.027	0.018	0.129	-0.189	-0.180	-0.028	-0.018	0.220	0.217	-0.035	-0.014	-0.080	-0.019

*. Correlation is significant at the level of 0.05 (2-sided)

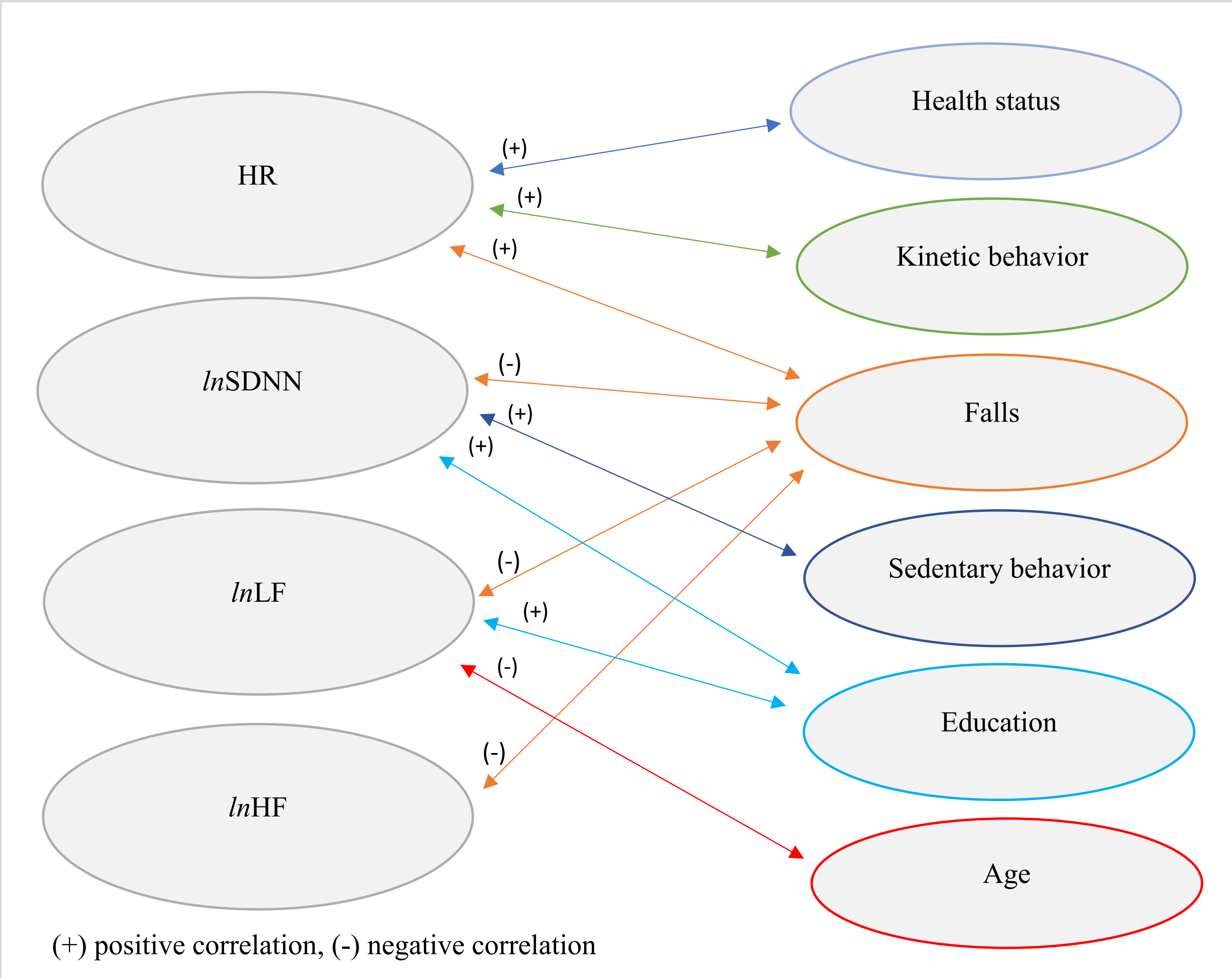

Figure 9: Correlations between lifestyle parameters and HRV parameters

3.5 COGNITIVE PERFORMANCE

Examining research question four due to cognitive abilities, possible differences between the groups and their performances had been identified. At first, group differences among the study groups were analyzed followed by a selection process to find predictors influencing cognitive processes.

3.5.1 GENERAL GROUP DIFFERENCES

Among the groups, a highly significant difference for STROOP3 was found by ANOVA analyses [$F(2,68)=9.642$, $p=<.001$, $\eta^2=.221$], which can be seen in Figure 10. Post-hoc tests showed a significant difference between the HFS group and the THA group p=.006, and between the HFS group and the control group p=<.001.

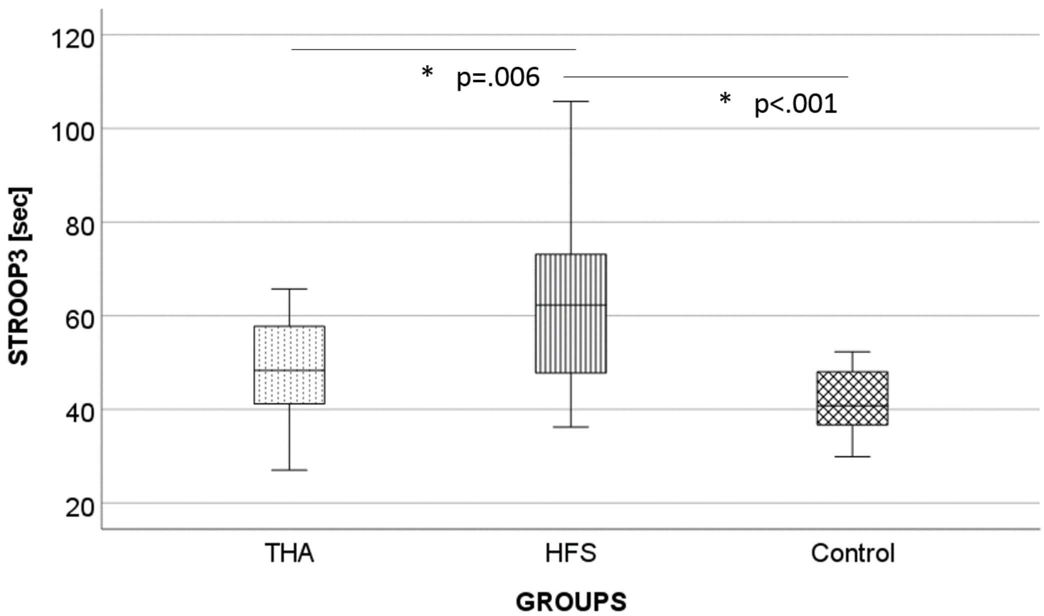

Figure 10: Differences among the groups in the parameter STROOP3

3.5.2 Selection process of predictors defining cognitive performance

The overall regressions model predicted approximately 52.2% of the variance in STROOP 3 [$F(13,70) = 4.783$, $p < .001$, adjusted $R^2 = .413$]. The predicted STROOP 3 of participants was equal to 60.768, - 9.276 (education), + 12.293 (eye disease), + 11.834 (fear of falls) and - 24.348 (*ln*HF_Base).
As seen in Figure 11 and Table 8, lower education, higher eye disease, higher fear of falls and lower *ln*HF_BASE predict higher reading time.

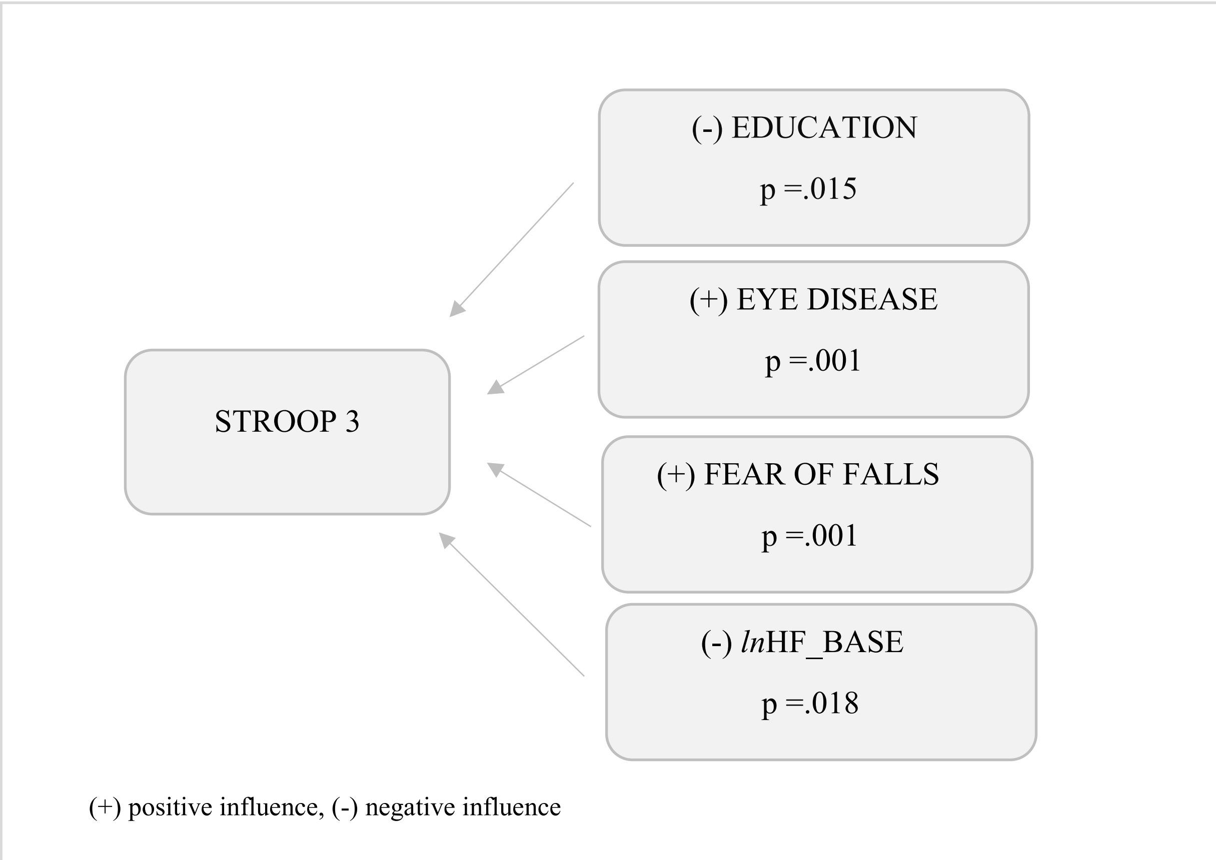

Figure 11: Results of regression analyses for predictors for STROOP3 test

Table 8: ANOVA results for evaluating predictors of cognitive performance

Model summary									
				Change Statistics					
	R	R Square	Adjusted R Square	Std. Error of the Estimate	R Square Change	F Change	df1	df2	SigF Change
	.722a	.522	.413	12.5170	.522	4.783	13	57	.000

a. Influencing variables : (constant), lnHF_Base, Kinetic behavior, Eye Disease, Education, Fear of falls, Sports kid, Health status, Income, LF/HF, Heart rate, lnSDNN Base, lnRMSSD Base, lnLF Base

ANOVA[a]					
	Sum of squares	Df	Mean Square	F	Sig.
Regression	9742.111	13	749.393	4.783	.000b
Residual	8930.476	57	156.675		
Total	18672.586	70			

a. Dependent variable: STROOP 3

b. Predictors: (Constant). lnHF_Base. Kinetic behavior. Eye Disease. Education. Fear of falls. Sports kid. Health status. Income. LF/HF. Heart rate. lnSDNN Base. lnRMSSD Base. lnLF Base

Coefficients

	Unstandardized Coefficients		Standardized Coefficients		95% Confidential Interval	
	Regressions CoefficientB	Std. Error	Beta	Sig	Lower bound	Upper bound
(Constant)	60.768	20.801		.005	19.115	102.421
Education	-9.726	3.872	-.284	.015	-17.481	-1.972
Income	1.608	4.039	.046	.692	-6.480	9.695
Eye disease	12.293	3.543	.376	.001	5.198	19.389
Kinetic behavior	.022	3.744	.001	.995	-7.475	7.519
Health status	-2.342	6.216	-.043	.708	-14.789	10.105
Sports kid	4.590	3.507	.141	.196	-2.434	11.613
Fear of falls	11.834	3.459	.359	.001	4.908	18.760
Heart rate	-.130	.191	-.097	.499	-.513	.253
LF/HF	-5.965	4.938	-.369	.232	-15.854	3.924
*ln*SDNN base	-4.570	9.100	-.147	.617	-22.793	13.653
*ln*RMSSD base	9.005	7.448	.407	.232	-5.910	23.919
*ln*LF base	12.523	17.873	.256	.486	-23.268	48.313
*ln*HF base	-24.848	10.189	-.793	.018	-45.251	-4.444

Dependent variable: STROOP 3

In the following figure 12, the duration of the STROOP3 testing is presented. The diagram shows the decrease of time with an increase of *ln*HF_Base, p=.018.

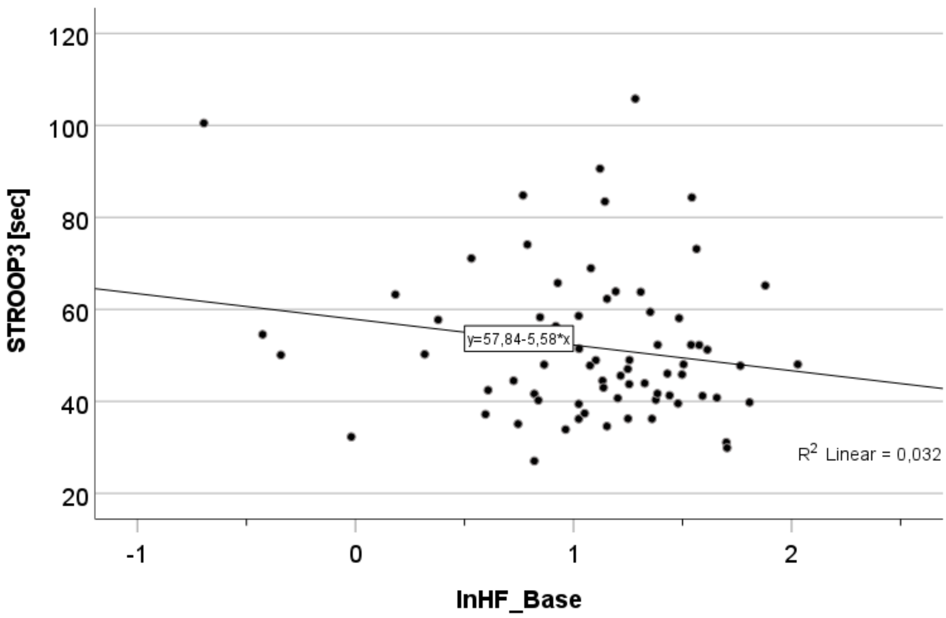

Figure 12: STROOP3 testing time correlated with lnHF_Base for the total groups

The duration of the STROOP3 testing time was higher in the group with low education on the basis of the total group p=.015, as shown in Figure 13.

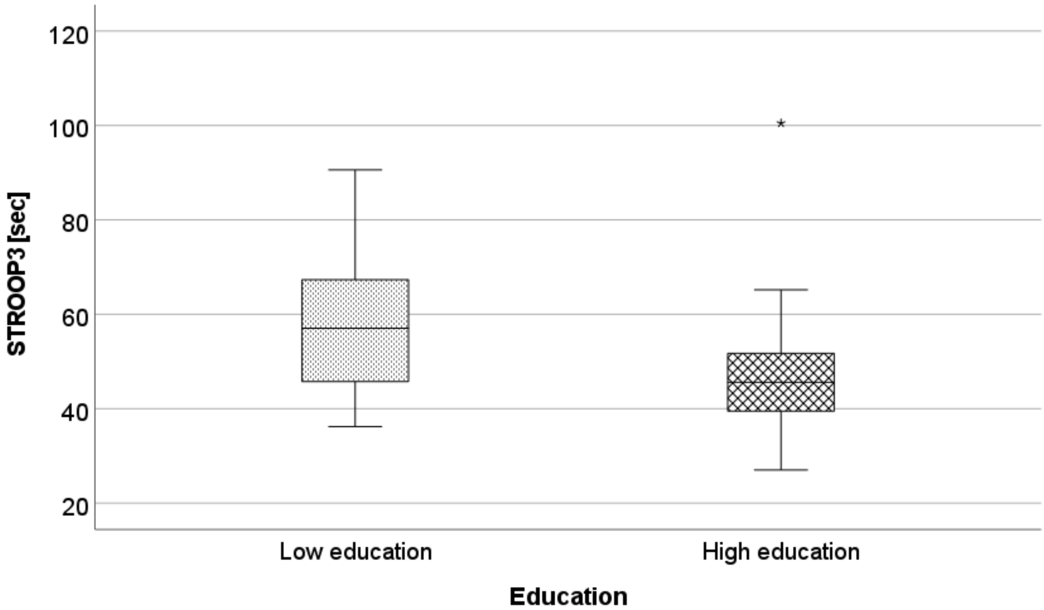

Figure 13: STROOP3 testing time correlated with education for the total groups

Among participants with eye diseases, STROOP3 testing time was higher p=.001, in relation to the total groups, as presented in Figure 14.

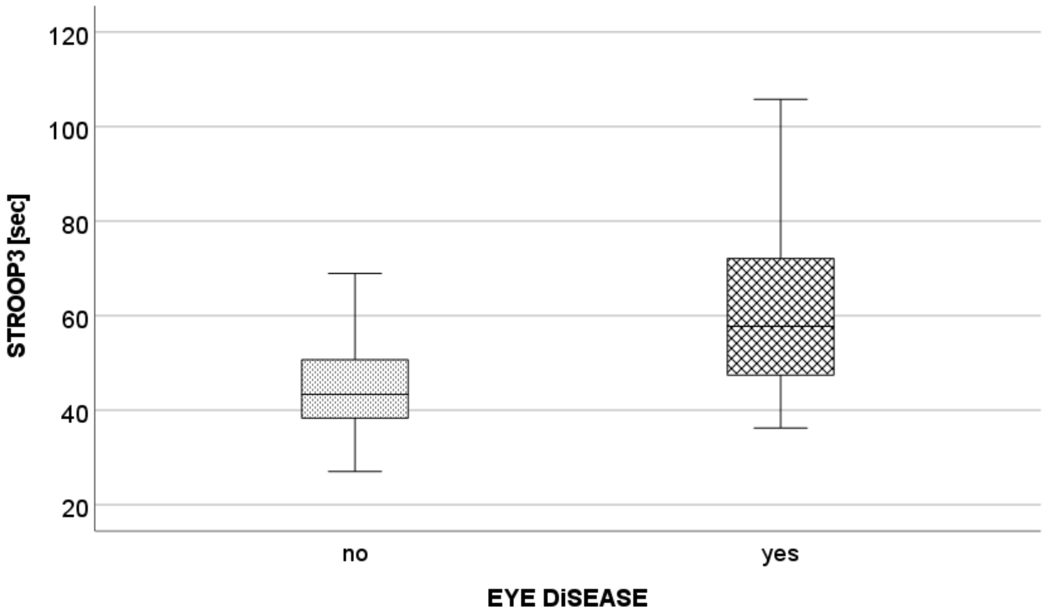

Figure 14: STROOP3 testing time of the total groups correlated with eye disease

STROOP3 testing time of the total groups was higher in participants with fear of falls p=.001 compared to their counterparts with no fear of falls, as demonstrated in figure 15.

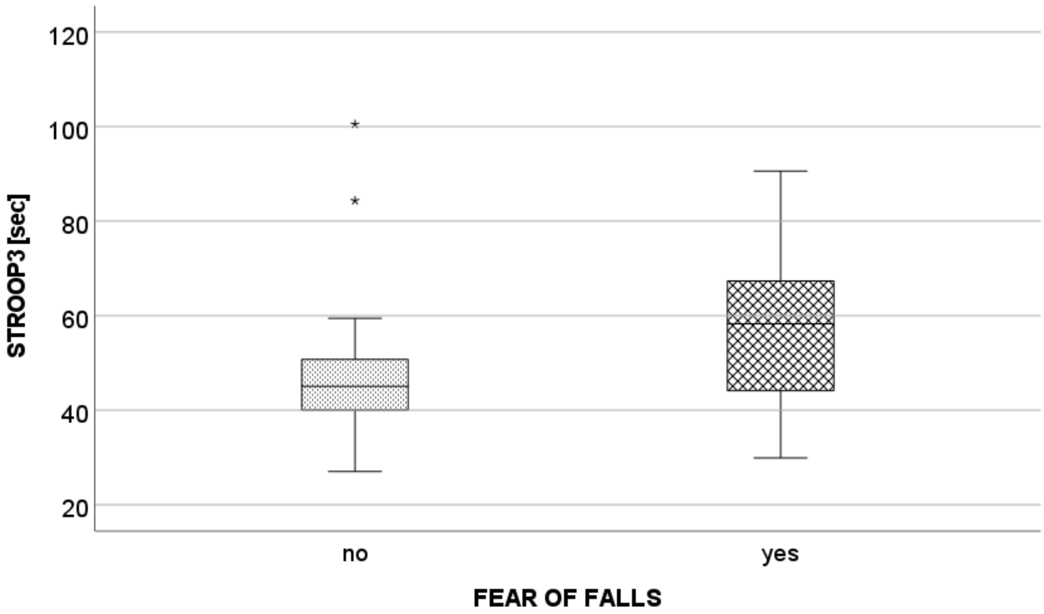

Figure 15: STROOP3 testing time of the total groups correlated with the parameter fear of falls

4 DISCUSSION

4.1 ANTHROPOMETRIC PARAMETERS

Anthropometric results of this study could reveal a possible differentiation of the HFS patients, THA patients and healthy participants – the control group – in various parameters like weight, BMI, CC and in the parameters SBP and DBP. Based on the results of the measurements, it could be seen that the HFS group had a poorer physical baseline compared to the other groups. Significant values were observed when detecting lower weight, lower BMI and higher blood pressure, SBP and DBP, in comparison with the THA group. Such a result has already been demonstrated with previous findings, showing that high BMI [203] or high weight [204] and high SBP confers to a higher risk of hip fractures [205]. In the same way, our results support the findings of these studies with the idea that a smaller CC has higher potential for hip fractures and a large percentage of prediction [117]. Another study by Singh et al. demonstrated a correlation between CC and bone mineral density, which strengthens the possibility of a higher incidence of hip fractures possibly being influenced by a maladaptive lifestyle [206].

4.2 DIFFERENCES IN LIFESTYLE BETWEEN THE GROUPS

Research question II explores differences in lifestyle parameters between the three study groups. The smoking parameter is particularly worth mentioning as being significant higher in the HFS group compared to the control group. In accordance with Wu et al., this study finds similar elaborations of the influence of smoking and the frequency of hip fractures [207]. A direct correlation between hip fractures and smoking was mentioned in a research project performed by Ampelas corresponding to our study, which considered the possible influence of smoking being an indicator of adverse life circumstances [208]. A further important factor influencing life and daily routines is the condition of the eye quality and the visual function. Poorer vision has a high risk of falls and fractures, as reported by Cox et al., which the present study can also demonstrate [59]. Likewise, Sun et al. and Loriaut et al. corroborate the results of this study by attesting hip fracture having a significantly more frequent indication of eye disease and poorer vision [209, 210]. Further, the available study can mention the parameter of physical activity, presenting a lifestyle shaped by movements. Highly significant results were observed in the HFS patients compared to the control group for being more inactive than the participants of the control group and significant values were seen in the HFS group compared to the THA group, similarly elaborated by Feskanich et al. showing that a moderate exercise program with weekly walking time was successful in hip fracture prevention [170]. Lageross et al. offered a similar result by presenting the association between hip fractures and physical activity [171]. Concerning other important aspects why physical activity and movements are not possible to be implemented in everyday life is the crucial point when people suffer from pain. The THA patients and HFS patients showed significantly higher sensations of pain compared to the control group, with the impact of being more impaired in their physical activity and movements. Pain influences everyday life extremely due to the impossibility of performing movements in one's daily routine, whereby the quality of life rapidly declines. Crawford and Murray found pain to be the principal indication of being operated, which this study can show based on highly significant results among the THA patients [64].

A major problem, clearly visualized in the group of the HFS patients is the fear of falling, walking along with limiting one´s everyday life. After one or more falls, people are afraid of falling again, which Visschedjik et al. investigated in their study drawing the picture of a connection between falling and a higher fear of falling in elder people [211]. In this investigation, the HFS group showed significantly higher results in the parameter fear of falling than the control group, which strengthens the results of the investigation by Visschedjik. A logical consequence of fear of falling is avoiding movements to avoid encountering a fall situation. This statement is possibly confirmed by Tinetti's investigation showing the influence of fear of falling in avoiding activities and physical movements [212].

4.3 Differences in HRV parameters between the groups

The results of the HRV analysis provide information about the state of health of an individual person at any time of a measurement situation. Therefore, this study can offer insights into the personal health situation of the probands of the various investigation groups analyzing HRV parameters. In almost every specific investigation of this study, HRV analysis results gave information about the personal health state of each member of the investigation groups whereby adverse findings primary were detected in the HFS group.

4.3.1 BASELINE CHARACTERISTICS

Initially, it can be determined that basic differences among the three study groups has been found. Baseline HR was the lowest in the control group, followed by the THA group and the highest in the HFS group. *ln*SDNN values at baseline were lower in the HFS group compared to the other groups. The results of *ln*LF and *ln*HF were similarly lowest at baseline in the control group and highest in the HFS group. These results are in accordance with previous studies showing that hip fracture is connected to lower HRV, demonstrating the higher fragility of patients [152, 213]. This might be explained by the aspect that a reduced HRV is linked to higher morbidity and mortality [137, 160, 161]. Ernst et al. first found significant associations between patients with hip fracture and pre-operative diagnosed low HF and low RMSSD indicating stroke and pneumonia, likewise a low SDNN and low LF and HF being related to higher mortality after hip surgery [165].

4.3.2 CHANGES OF PARAMETERS OVER TIME

A second consideration of this investigation offered insights into the time course and the challenges at a special time point presenting significant differences in the collected and analyzed HRV data. The values of the HRV parameters changed in the normal range according to the challenge of the respective specification combined with the temporal course of this investigation, as seen in the study by Michael et al. denoting the change of the values related to the different stages of an exercise [214]. This investigation showed highly significant results in all parameters of the HRV analysis over time, except the *ln*HF parameter. As an example, HR increased during the GS challenge and declined after a resting time to an approximate value of the initial value. This is in accordance with Cole et al. showing that an abnormal HR recovery after exertion is expelled as a predictor of death [215]. It is an interesting observation that HR fully recovers but parameters of the HRV analyses didn´t behave in this way. The time scale of HR and HRV recovery appears to be obviously different in their process operations. Regulation of HR is not the same as regulation of HRV showing that the recovery of the HRV possibly needs more time to decrease to the initial value. Based on these results, it must be taken into account that body composition can have an influence on stress reactivity and consequently on HRV. Overweight people can show increased stress reactivity compared to normal weight people what was found and validated by Chandola et al. by finding an association between stress and lower HRV [216].

The sympathetic regulation expressed by the parameter LF has not recovered to the baseline level. A further study would be necessary to investigate this divergent process in more detail. It can be said that this analysis could possibly offer valuable insights into HRV analysis and their parameters showing the sensitivity to any physiological changes in diverse parts of stress response [217].

4.3.3 Interaction effect between time and group

The interaction effect between the groups in the *ln*SDNN parameter demonstrated a significantly difference over time between the HFS group and the control group. This result demonstrates the regulation of the interplay between the sympathetic and the parasympathetic nervous systems. The HFS group exhibited lower *ln*SDNN values than the control group possibly being a result of a different lifestyle. This is in accordance with Emili et al. denoting a higher SDNN arising from a higher HRV, which is significant for a better lifestyle by having integrated exercise programs for more stability and sustainability for a healthy life [218]. The low *ln*SDNN of the HFS group offers possible hints at an inactive lifestyle, which can be compared with the study of Felber et al. demonstrating the association of an inactive lifestyle, explaining itself by avoiding movements in everyday life, and the risk of suffering cardiovascular diseases by heart failure [219]. These results from a lack of mobility, meaning reduced exercise behavior and increased sitting time, as reduced mutual fitness leads to a degraded ability to react in situations where a high probability of falling is given, and which in turn can contribute to a frequency of falls, as shown in the study of Morseth et al. [220]. Another perspective is based on the body composition, depicted by the anthropometric parameters and the association with HRV, based on stress and recovery results, elaborated by Teisala et al. showing the association between stress and HRV indicators and body composition as an important indicator of a healthy lifestyle [168]. For this reason, the study group with the worst results of the HRV analysis – the HFS group – should be devoted special efforts in life-changing areas for better outcomes after surgery and the avoidance of new falls.

Furthermore, the results showed also a trend to significance by the interaction effect in the parameter HR which showed a significant post hoc test between the HFS group and the control group. The borderline significance may be due to a small sample size. In this context it must be stated that the HFS group showed higher HR baseline values compared to the other intervention groups. Wang et al stated that higher HR is associated with all-cause mortality and can be applied as a prognostic marker [221]. This effect could possibly indicate that high HR and HR changes show to be a sign of stress or of poor physical condition and as well contributing to falls [222]. Lifestyle in this connection addressed by Faulkner et al. found an independent association with falls denoting the environmental and behavioral risk factors being important causes of falls [223]. Worthy to mention is the higher number of women in the HFS group and the possible fact that these women potentially didn´t press the GS dynamometer as strong as possible due to surgical weakness or inability because of bad health conditions. To make this situation more transparent a personal pressing protocol could be taken for further studies to standardize this special part of the investigation.

4.4 Relationship between lifestyle and cardiovascular parameters

The relationship between an active lifestyle and diseases concerning the heart and the circulatory system are widely subject to research. The present study approached this topic by defining this question at hand, realizing a main emphasis in the selected intervention groups.

4.4.1 Significant correlation analyses results

Several parameters were found to show the connection between lifestyle and HR and HRV. In the following, each HRV parameter that was found to be significant in some way is presented separately to maintain the importance of this intervention. The relevance of such an analysis provides information for having topics to prevent negative outcomes in the elderly population by analyzing HRV as a dynamically influencing system of the PNS and SNS [224]. This investigation showed a positive correlation with health status, falls and kinetic behavior. Health status – here personally defined and described based on the present perception – is decisive for a better quality of life [225]. The positive correlation between HR and health status, the better HR (lower HR baseline) is the better is the health status, provides information of the importance of body and brain fitness, as elaborated by Rammath et al., which could be confirmed by this study [226]. The connection of body training, inducing a higher flexibility of heart rate adaption, and the well-being of elder people was reported by Batista et al. and fits well to our study [225]. The frequency of falling in the elder population was given throughout the positive correlation with HR, the higher HR the higher the incidence of falls. The present study has detected that people with falls showed higher HR baseline. This arises from the motion that the better that the cardiovascular system is working, the fewer falls that will be recorded. This is in accordance with Goswami et al. diagnosing falls as a major problem correlating with a higher HR and HRV [227]. The association between depressed HRV and a higher risk of falling was found by Melillo et al. [228]. The correlation between these two parameters was given due to low movement behavior, which indicates the immobility of those test persons who have a higher tendency to falls. Tan et al.'s findings are in line with the outcome of these results, namely falls being caused by cardiovascular disorders [229]. The outcome of the correlation analysis provides positive results for kinetic behavior, showing probands being restricted in movements with the adaptive ability to the task presenting a higher HR. The connection between HR baseline and kinetic behavior is shown in the study of Christofaro et al. denoting HR baseline as an indicator for cardiovascular health by showing that a higher HR baseline is associated with a lower kinetic behaviour which is in agreement with the results of the correlation analysis of this study [230].

A further result of the correlation analysis is shown by the HRV parameter *ln*SDNN, providing information about the overall variability of the heartbeat. It shows how well the nervous system can regulate processes in the body. Education showed a weak positive correlation by showing the better the education level, the higher the *ln*SDNN value. A direct relationship with high education and high *ln*SDNN is observed. Education is linked with stress, how to manage stressful situations like exams or other stressing occasions like speaking in front of a group or presenting a topic. Malik et al. presented HRV as an established method to measure fluctuations of the sympathetic and parasympathetic nervous system as well in healthy individuals as in people with cardiovascular and non-cardiovascular disorders [231].Therefore, this study was using this established measure to test it on the available subjects. Köllner et al. showed that a high HRV at rest means adaptive emotion regulation, self-regulation and better self-esteem [232]. These elaborations were observed in this study as being more relaxed – denoting a higher SDNN – correlated with higher education.

The more that, one person showed a higher SDNN, having a high modulation of the vagal and sympathetic branch of the nervous system, the more vitally a person was managing their life. This indicates an ambitious lifestyle, which strengthens the theory of Buchheit et al. that elderly people with a sporty lifestyle have a higher HRV and vagal-related indexes [233]. These results can relate to our study by denoting reduced falls with higher results in the *ln*SDNN parameter. The correlation analyses of the *ln*LF parameter revealed weak results with lifestyle parameters. LF mostly determined sympathetic modulation, while others interpret it as a combination of sympathetic and parasympathetic activity. The consensus is a mixture of both autonomous inputs. In practical terms, an increase in the LF component (peak performance, mental and/or physical stress, sympathomimetic pharmacological substances) was generally viewed as a result of sympathetic activity. Falls are negatively correlated with LF, showing the expected outcome of an enhanced lifestyle with a lower LF outflow combined with a lower incidence of falls what was confirmed by Buchheit et al. mentioning that a long-term sporty lifestyle counteracts the age-related decline of vagal HRV (HF, RMSSD) better than a sedentary behavior combined with an increased tendency to fall [233]. This is in accordance with Terroba-Chambi et al. suggesting that higher sympathetic results were associated with higher risks of falls [234]. Age-related changes of HRV and especially a reduced LF in comparison to high age was observed by Stein et al. concluding that HRV is affected by age, denoting that for older people a higher reduction of HRV was observed [235]. Elaborations of this study show similar outcomes, whereby the higher the age, the lower the result of LF. The study by Zhang et al. demonstrated the strong impact of age on HRV by showing the older the probands were, the lower was the HRV [236].

A further correlation was observed between *ln*HF and falls. In this investigation, the correlation was weakly negative, defining that the lower the *ln*HF results were, the higher was the probability of suffering a fall. The HF component is generally defined as a marker for vagal modulation. This component is breath-mediated and therefore determined by the respiratory rate. Hernando et al. showed that HF decreased during stress and is mediated by breathing, giving a more reliable characterization of the autonomic nervous response to stress [237]. Furthermore, Shaffer et al. were able to demonstrate the connection between reduced HF and stress, which is in accordance with the outcomes of this study, finding lower *ln*HF values possibly being related to higher occurrences of falls [150]. Stress induces potentially falls, which was observed in this investigation by lower *ln*HF being linked to a higher incidence of falls. Fink et al. found that stress has an impact of an increased risk of falls, which this study supports by higher values of falls with lower *ln*HF [238].

4.5 Cognitive performance

In order to find differences among the intervention groups, a selection process was adapted. Therefore, a STROOP3 test was introduced as a probate instrument to determine the cognitive performance of the patients.

4.5.1 General group differences

The question arises whether HFS patients have more cognitive function deficits compared to the other intervention groups. Related to our results, a clear assignment can be made. ANOVA results showed a significant difference in the results of the HFS group compared with the THA group and the control group. In the search for a possible explanation, we can suggest that the HFS group is slower in its reading speed than the other groups. This means that the reproduction of reading a text abstractly – as it is expected in the STROOP3 test – is slower than in the other groups. This test is associated with cognitive impairment [239], which in turns lead to more falls [240]. Cognitive impairment is the primary exposure to fall risk, which can be confirmed in this study by our results [126]. The HFS group took the longest measured time to complete the STROOP3 test (interference test) compared to the other groups, which indicates the poorer cognitive efficiency of this group. This is in accordance with Gruber-Baldini et al. denoting the association between falls and cognitive measures [241]. The connection of falls and cognitive impairment as well as the attribute of being in a special age range is subject to a vast body of research, picturing the need for a geriatric assessment for better outcomes after a hip operation [242].

4.5.2 Selection process of predictors defining cognitive performance

This study has the possibility to explore the important question of finding predictors for cognitive efficiency among the study population. The results of the STROOP3 test – the interference test – elaborated four parameters for being important as a predictor of being assigned as cognitively impaired. As mentioned above, this in turn leads to more falls and thus an increased incidence of hip fractures. The following factors predicting the STROOP3 test could be found out: education, eye disease, fear of falls and *ln*HF_Base.

The results of this study showed that a higher level of education was related to a shorter reading time. In the study by Ye et al., a slower cognitive decline at the early stage of a mild cognitive impairment was observed in the group with higher education than in the group with lower education [243]. This result was supported by Amieva et al. and shows a protection of higher education against further cognitive decline [244]. Therefore, the present study can also contribute to these results.

A relationship between cognition and eye diseases has been proven in various hypotheses to find correlations between brain function and vision. The STROOP test is respected as a golden test comprising different tasks and it is highly involved as a visual input measurement [245]. The results of this research are in line with Daniel et al. denoting a longer accommodation period and a higher error rate by probands with eye diseases, which the results of this elaborations can support [246]. Participants in this study with eye diseases showed a higher reading time compared to people with less eye diseases. The connection with a slower reading time was essentially evoked by a longer fixation time, which strengthens the correlation between cognition and vision.

Another result of the regression analysis of this study in terms of finding predictors for the STROOP 3 test is fear of falls. Nearly with the same result as for eye disease, fear of falls correlates with extended reading time on the STROOP3 task. It emerges that those test persons who needed more time to read the STROOP3 task also had an increased fear of falling. This connection is confirmed by Vo et al. and Hoang et al. and closely linked with the consequences of increasing age, namely a mental and functional decline [247, 248]. One of the main problems is the avoidance of daily activities, which weakens the bones and body health of elder people [249]. The relationship between cognitive impairment and fear of falls was as well represented as confirmed by this study and was even worth being a predictor of STROOP3. Through the outcome of this study, the assumption is obvious to pay more attention cognitive and physical trainings for the elderly within intervention programs [250].

The fourth parameter elaborated and established as a predictor of the STROOP3 test is a parameter of the HRV analysis, namely *ln*HF_Base. This parameter significantly correlates with the STROOP3 test and was the only HRV parameter that emerged as a predictor of cognitive impairment. The lower the HF, the higher the risk of stress, anxiety, and cardiac disease, resulting in increased morbidity [251]. This study possibly goes along with ongoing research denoting that the lower the *ln*HF_Base was, the higher was the reading time of the STROOP3 test. This is in accordance with Forte et al. considering HRV as an early biomarker for cognitive impairment [252]. It has been observed in literature that the HF of the HRV analysis was the most frequently-reported parameter [253]. The intervention groups of this study showed a lower *ln*HF_Base and a higher reading time in the STROOP3 test. This indicates a possibly worse result for the required task, signifying a group of probands with the need for special attention [254]. A reduction of the vagal tone – reduced HF in the HRV analysis – can be realized as a deficit in terms of being flexible to changing demands. For this reason, this investigation holds a possible importance, pretty easy showing deficits based on simple recorded measurements. However, caution must be applied by interpreting these results of the regression due to the small explained variance, R^2. An association of a small amount has been observed which could be a possible predictor under other conditions. Indeed, this limits the conclusion drawn and warrants further studies about the suitability of this HRV parameter as predictor.

It should be noted that this study – which focused on the comparison and possible relationships between various parameters of hip-operated patients and a non-operated group – has limitations to be considered. As previously mentioned, this study pointed to the special aspect of two hip-operated groups being compared to a control group in relation to various factors. When selecting test persons, it must be mentioned that the group of non-operated test persons – who were addressed personally and came from a certain, quite homogeneous environment – could not reasonably be compared with a sample that was estimated at random. Diverse results could have been found generating a more random sample; for example, asking any people encountered in the hospital area. This possibly placed a limit in the selection process and potentially had an effect on a wider interpretation in this field, placing a limit in the selection process with the conceivable effect of a wider interpretation in this field. Further, it has to be considered that the sample size in each group was small. Although the number of participants was large for the estimated selection period, a considerable number of participants of the HFS group had to be excluded or withdrawn from the study due to pathological issues. Due to not being able to sit quietly during ECG recordings and due to deficient execution of the instructions for the leading point of the investigation, participants were unable to carry out the procedure of the investigation process consistently. Therefore, it is obvious that patients in the HFS group can possibly limit a representative picture of the traumatic ward. Furthermore, we conducted our experiment with patients from one single hospital in Austria, being medically treated for hip fracture or hip arthritis and compared these patients with healthy adults. These data thus could scarcely be generalized to the overall population of patients being medicated for hip fracture or a surgery due to painful and restraining arthritis in the hip joint. A further limitation was a possible response bias, whereby participants might have provided a false reflection to questions of the approved questionnaire to avoid disappointing the head of the investigation or to maintain an image of being a “better patient”. Real activity data using an accelerometer to receive physical activity data could give more insights into the present state of health of a participant than a self-completed questionnaire. Another possible limitation might be the selection of confounders that affect HRV variables such as the respiratory rate, which was not measured and analyzed in this study as well as during ECG recordings. Consequently, future research should focus on a broader sample with a one-to-one analogy related to sex and age. In further studies, a larger number of participants should be included, possibly with different entrance criteria, such as an open upward age limit or additional ECG recording options, such as pre-operative ECG reports or data records at time of admission. The use of a more representative group of the traumatic ward is warranted and the sample should be taken from more hospitals, not limiting the generalization and the transferability in all settings. Therefore, a multidisciplinary study might be needed in further research for a wider validity.

5 Conclusion

Lifestyle is a term often used in connection with health and longevity, and it is important for the healthcare resources of the aging population as well as being related to healthcare costs. Through lifestyle, people can influence possible health developments at an early stage gaining a better health-seeking behavior.

Likewise, the measurement of HRV and the analysis of different and informative variables that are able to show an effect on the current health state of a person are important, offering insights and perspectives into possibly upcoming diseases. Therefore, this study investigated two groups of patients with hip surgery – HFS and THA – and a control group to find differences in lifestyle as well as anthropometric and cardiovascular parameters regarding their implications. The results illustrate the sensitivity of the autonomic nervous system and show that a large number of influencing factors should be taken into account so that comparisons can be made between groups (patients, control group) for which HRV can be used as a proven measuring instrument. Significant differences were observed in diverse lifestyle aspects, in cardiovascular parameters and relationships between lifestyle and HRV parameters among the study groups. The analysis of HRV parameters revealed a significant interaction effect in the HRV parameter *ln*SDNN between the HFS group and the control group. A correlation between lifestyle factors and cardiovascular variables showed positive effects between the parameters health status, kinetic behavior and falls and HR, sedentary behavior and education and *ln*SDNN, education and *ln*LF and negative effects between the parameters falls and *ln*SDNN, falls and age and *ln*LF and falls and *ln*HF. Cognitive impairment is proven to be a negative prognostic factor for the recovery of mobility in older patients with a hip operation. For this reason, a cognitive performance test – the STROOP test – was conducted with the result of significant differences among the study groups. Predictors for one of the parameters, the STROOP3, were found after regression analysis and showed a positive influence in eye disease and fear of falls and a negative influence in education and *ln*HF_Base. These results can possibly give a suggestion of new aspects and improvements in treatment and prediction. HRV measurements combined with measurements of lifestyle parameters provide additional information beyond the state of health and could be used to identify relevant lifestyle factors of a person to improve their everyday life. The present investigation, performed by non-invasive measurements, has the impact to detect health deficits of a patient at an early stage related with the chance to steer the patient in a positive direction possibly effected by lifestyle changes. Hence, this study may offer new insights into research and its questions due to the lifestyle of hip-operated elderly people, closing a gap in literature with the main interest in exploring the relationships between HRV and lifestyle of the mentioned patient groups. Further research is needed to confirm the present results of this study in a larger cohort of hip surgery patients and to add to a dynamic and constantly growing database of specific guidelines and cut-offs for HRV parameters. Concluding, HRV analysis can be used as a tool in everyday clinical practice to obtain information about a patient's resilience and need for intervention.

6 References

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7 APPENDIX

7.1 CASE REPORT FORM

Datum (TT/MM/JJJJ) ____ / ____ / ________

STAMMDATENBLATT

Familienname/Vorname(n) _

Geburtsdatum _

Maße Körpergröße: cm Körpergewicht: kg

Probanden-ID: ☐☐

Termin	Uhrzeit	**Kontaktdaten**
Untersuchungstermin		Telefon
		E-Mail
		Adresse

Ein- und Ausschlusskriterien

Einschlusskriterien	**ja**	**nein**
Schriftliche Einwilligungserklärung	☐	☐
Alter: 60 ≥ und ≤ 85 Jahre	☐	☐
Sprachfähigkeit - Deutsch	☐	☐
BMI < 35	☐	☐
Medialer Schenkelhals post OP/ Prox. Femurfraktur post OP **oder**	☐	☐
Cox Arthrose post OP	☐	☐
Gesunde Gruppe	☐	☐

Ausschlusskriterien	**ja**	**nein**
Patienten mit Demenz und schweren kognitiven Einschränkungen	☐	☐
Neurodegenerative Erkrankungen (Morbus Parkinson, etc.)	☐	☐
Autoimmunologische Erkrankungen (Multiple Sklerose, etc.)	☐	☐
Schwere visuelle und/oder auditive Einschränkungen	☐	☐
Sonstige Gründe, wie Drogen- und Alkoholabusus sowie fehlende Compliance	☐	☐
Schwere organische Einschränkungen, die den Ablauf oder Fortgang der Studie negativ beeinflussen könnten	☐	☐

Aktuelle Erkrankung/en

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Bemerkungen

____

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____

Korrelation zwischen sitzendem Lebensstil, sturzbedingten Verletzungen und kardiovaskulärer[1] Reaktionsdynamik

Sehr geehrte Teilnehmerin, sehr geehrter Teilnehmer!

Wir laden Sie ein an der oben genannten Beobachtungsstudie teilzunehmen. Die Aufklärung darüber erfolgt nun in einem ausführlichen Gespräch.

Ihre Teilnahme an dieser Studie erfolgt freiwillig. Sie können jederzeit ohne Angabe von Gründen aus der Studie ausscheiden. Die Ablehnung der Teilnahme oder ein vorzeitiges Ausscheiden aus dieser Studie hat keine nachteiligen Folgen für Ihre medizinische Betreuung.

Beobachtungsstudien sind Studien, bei denen in der Regel nur Daten aufgezeichnet und ausgewertet werden, die im Rahmen der normalen Patientenversorgung anfallen. In manchen Fällen kann es auch sein, dass zusätzliche, nicht belastende Untersuchungen oder Befragungen vorgenommen werden. In keinem Fall wird die für Sie vorgesehene Behandlung durch Ihre Studienteilnahme verändert. Beobachtungsstudien sind notwendig, um zusätzliche Erkenntnisse über bereits bewährte medizinische Verfahren zu gewinnen.

Bitte unterschreiben Sie die Einwilligungserklärung nur

- wenn Sie Art und Ablauf der klinischen Studie vollständig verstanden haben,
- wenn Sie bereit sind, der Teilnahme zuzustimmen und
- wenn Sie sich über Ihre Rechte als Teilnehmer an dieser klinischen Studie im Klaren sind.

Zu dieser Beobachtungsstudie, sowie zur Patienteninformation und Einwilligungserklärung wurde von der zuständigen Ethikkommission eine befürwortende Stellungnahme abgegeben.

Was ist der Zweck dieser Studie?

[1] Kardiovaskulär – das Herz-Kreislaufsystem betreffend.

Der Zweck dieser Beobachtungsstudie ist das Ermitteln der unterschiedlichen Reaktion des Herz-Kreislaufsystems zwischen den Patienten nach Oberschenkelbruch und Schenkelhalsfraktur oder Cox Arthrose (Gelenkerkrankung der Hüfte). Dies soll in einer kurzen Untersuchung ermittelt werden, in der die Reaktion des Herz-Kreislaufsystems unter Ruhe und bei einfachen Belastungen (wie z.B. Wortleseübungen und Handkrafttest) in seiner Veränderung beobachtet wird. Für die Ermittlung biologischer und physiologischer Parameter kommen Fragebögen zur Anwendung (Lifestyle, Gesundheitszustand etc.). Es gibt wissenschaftliche Hinweise, dass diese Parameter miteinander in Zusammenhang stehen und dass diese unser Leben beeinflussen können.

Wie läuft diese Beobachtungsstudie ab?

Ihre Teilnahme an dieser klinischen Pilotstudie ist freiwillig und ich danke Ihnen, dass Sie vorhaben, sich dafür zur Verfügung zu stellen. Während der Dauer dieser Studie werden Sie von mir betreut und in den Übungsabläufen unterstützt und ermutigt.

Diese Studie wird am Klinikum Graz – Abteilung für Unfallchirurgie – durchgeführt und es werden ungefähr 60 Personen daran teilnehmen. Ihre Teilnahme wird Sie ungefähr 45 bis 50 Minuten beanspruchen.

Folgende Maßnahmen werden ausschließlich aus Studiengründen durchgeführt:

Zu Beginn werden Sie gebeten Fragebögen auszufüllen. Ich werde danach Ihren Wadenumfang messen und Ihnen einen Gurt zur Messung der Atemfrequenz (Atemzüge pro Minute) anlegen. Anschließend werden drei Elektroden für die EKG-Messung (Aufnahme der elektrischen Aktivität der Herzmuskelzellen) angebracht und es wird der Blutdruck, sowohl am Beginn als auch am Ende der Untersuchung mittels Manschette am Oberarm gemessen. Am Finger ist während der gesamten Untersuchung ein Pulsmesser befestigt. Es folgt ein Lesetest und nach einer kurzen Ruhephase wird Ihre Handkraft mit einem Gerät gemessen. Abschließend erfolgt nochmals eine kurze Ruhephase, um Ihre Herzaktivität in dieser Situation zu ermitteln. Die gesamte Untersuchung findet in sitzender Position statt.

Worin liegt der Nutzen einer Teilnahme an dieser Studie?

Durch diese Studie soll nachgewiesen werden, dass die kardiovaskuläre Reaktionsdynamik (Reaktion des Herz-Kreislauf-Systems) bei Patienten nach Oberschenkelbruch oder Schenkelhalsfraktur (postoperativ) und Patienten nach Cox-Arthrose (postoperativ) sowohl in ruhender Position als auch in Aktivität unterschiedlich verläuft. Es wird auf Lebensstil, Sitzverhalten und Sturzhäufigkeit Bezug genommen. Daraus soll sich dann eine Empfehlung zur Vermeidung von Stürzen ergeben.

Es ist nicht zu erwarten, dass Sie aus Ihrer Teilnahme an dieser Studie einen unmittelbaren gesundheitlichen Nutzen ziehen werden, aber möglicherweise werden künftige Patienten mit der gleichen Erkrankung von den Ergebnissen profitieren.

Gibt es Risiken, Beschwerden und Begleiterscheinungen?

Zusätzliche Einnahme von Arzneimitteln?

Hat die Teilnahme an der klinischen Studie sonstige Auswirkungen auf die Lebensführung und welche Verpflichtungen ergeben sich daraus?

Was ist zu tun beim Auftreten von Symptomen, Begleiterscheinungen und/oder Verletzungen?

Sollten im Verlauf der klinischen Studie irgendwelche Symptome, Begleiterscheinungen oder Verletzungen auftreten, müssen Sie diese Ihrer Studienleiterin umgehend mitteilen, ggf. telefonisch (Telefonnummern, etc. siehe unten).

Wann wird die klinische Studie vorzeitig beendet?

Sie können jederzeit auch ohne Angabe von Gründen, Ihre Teilnahmebereitschaft widerrufen und aus der klinischen Studie ausscheiden ohne dass Ihnen dadurch irgendwelche Nachteile für Ihre weitere medizinische Betreuung entstehen.

Ihre Studienleiterin wird Sie über alle neuen Erkenntnisse, die in Bezug auf diese klinische Studie bekannt werden, und für Sie wesentlich werden könnten, umgehend informieren. Auf dieser Basis können Sie dann Ihre Entscheidung zur weiteren Teilnahme an dieser klinischen Studie neu überdenken.

Wie werden die im Rahmen dieser Beobachtungsstudie gesammelten Daten verwendet?

Sofern gesetzlich nicht etwas anderes vorgesehen ist, hat nur die Studienleiterin und deren Mitarbeiter Zugang zu den vertraulichen Daten, in denen Sie namentlich genannt werden („personenbezogene“ Daten). Weiter können ggf. Beauftragte von in- und ausländischen Gesundheitsbehörden, der zuständigen Ethikkommission und Personen, die von der Studienleiterin dieser Studie mit der Kontrolle der Datenqualität betraut wurden, Einsicht in diese Daten nehmen, um die Richtigkeit der Aufzeichnungen zu überprüfen. Diese Personen sind zur Verschwiegenheit verpflichtet.

Die Weitergabe der Daten erfolgt ausschließlich zu statistischen Zwecken und Sie werden ausnahmslos nicht namentlich genannt. Auch in etwaigen wissenschaftlichen Veröffentlichungen der Daten dieser Studie werden Sie nie namentlich genannt werden. Sie haben jederzeit die Möglichkeit vom Widerrufsrecht zur Verwendung Ihrer Daten Gebrauch zu machen.

Die Bestimmungen des Datenschutzgesetzes in der geltenden Fassung werden eingehalten.

Entstehen für die Teilnehmer Kosten? Gibt es einen Kostenersatz oder eine Vergütung?

Durch Ihre Teilnahme an dieser klinischen Studie entstehen für Sie keine zusätzlichen Kosten. Ein Kostenersatz bzw. allfällige Vergütungen für die Teilnahme an dieser klinischen Studie sind nicht vorgesehen.

Möglichkeit zur Diskussion weiterer Fragen.

Für weitere Fragen im Zusammenhang mit dieser Studie stehen Ihnen Ihre Studienleiterin und ihre Betreuer gern zur Verfügung.

Name der Kontaktperson: Mag. Regina Csanády-Leitner

Erreichbar unter: 0316 385 81720

Einwilligungserklärung

Name des Patienten in Druckbuchstaben: ....

Geburtsdatum: .... Code: ....

Ich habe dieses Informationsblatt gelesen und verstanden. Alle meine Fragen wurden beantwortet, ich hatte ausreichend Zeit mich zu entscheiden und ich habe zurzeit keine weiteren Fragen mehr.

Mit meiner persönlich datierten Unterschrift gebe ich hiermit freiwillig mein Einverständnis, dass meine Daten gespeichert und ohne direkten Personenbezug für wissenschaftliche Zwecke verwendet werden dürfen. Mir ist bekannt, dass zur Überprüfung der Richtigkeit der Datenaufzeichnung Beauftragte der zuständigen Behörden und der Ethikkommission, sowie mit der Kontrolle der Datenqualität beauftragte Personen Einblick in meine personenbezogenen Krankheitsdaten nehmen dürfen.

Ich weiß, dass ich diese Zustimmungen jederzeit und ohne Angabe von Gründen widerrufen kann.

Eine Kopie dieser Patienteninformation und Einwilligungserklärung habe ich erhalten. Das Original verbleibt beim Studienleiter.

....

Datum und Unterschrift des Patienten

....

Datum, Name und Unterschrift der verantwortlichen Studienleiterin

(Der Patient erhält eine unterschriebene Kopie der Patienteninformation und Einwilligungserklärung, das Original verbleibt im Studienordner der Studienleiterin)